

**IN THE UNITED STATES DISTRICT COURT  
FOR THE EASTERN DISTRICT OF PENNSYLVANIA**

IN RE: GLUCAGON-LIKE	:	CIVIL ACTION
PEPTIDE-1 RECEPTOR AGONISTS	:	
(GLP-1 RAS) PRODUCTS	:	
LIABILITY LITIGATION	:	
	:	MDL No. 3094
	:	24-md-3094
THIS DOCUMENT RELATES TO:	:	
	:	HON. KAREN SPENCER MARSTON
ALL ACTIONS/ALL CASES	:	

# MEMORANDUM

**Marston, J.**

**August 15, 2025**

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This MDL involves personal injury actions stemming from the use of glucagon-like peptide-1 (GLP-1) receptor agonists and GLP-1/glucose-dependent insulintropic polypeptide (GIP) dual receptor agonists (collectively, “GLP-1 RAs”) manufactured by the Novo Nordisk Defendants (“Novo”)<sup>1</sup> and the Eli Lilly Defendants (“Lilly”).<sup>2</sup> (*See generally* Doc. Nos. 1, 294.) Eight GLP-1 RA medications are at issue: Ozempic, Wegovy, Rybelsus, Victoza and Saxenda, which are manufactured by Novo; and Trulicity, Mounjaro, and Zepbound, which are manufactured by Lilly.<sup>3</sup> The Court previously ordered early discovery and motion practice on three cross cutting issues, the first of which considers whether a physician can reliably diagnose a patient with gastroparesis without performing a gastric emptying study (“Cross Cutting Issue No. 1”). (Doc. No. 235 at 3–5.) Plaintiffs have put forth two experts on this issue, Daniel L. Raines, MD, FACG, and Eliot L. Siegel, MD, and Defendants have put forth one, Linda Nguyen, MD. Currently before the Court are Defendants’ motions to exclude the opinions of Drs. Raines and Siegel (Doc. Nos. 360–61) and Plaintiffs’ partial motion to exclude the opinions of Dr. Nguyen (Doc. No. 359).

## **I. BACKGROUND**

As of the date of this Memorandum, there are more than 2400 cases included in the MDL (*see* July 29, 2025 Hr’g Tr. at 25:22–24), but members of Plaintiffs’ leadership team have

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<sup>1</sup> The Novo Nordisk Defendants are Novo Nordisk A/S and Novo Nordisk Inc. (*See* Doc. No. 294 at ¶¶ 15–17.)

<sup>2</sup> The Eli Lilly Defendants are Eli Lilly and Company and Lilly USA, LLC. (*See* Doc. No. 294 at ¶¶ 20–21.)

<sup>3</sup> Although the Judicial Panel on Multidistrict Litigation (“JPML”) has not identified Victoza and Zepbound by name when transferring cases to be part of this MDL, the parties agree that they are properly included in this MDL. (*See* Apr. 4, 2025 Hr’g Tr. at 6:2–7:1.) Notably, Victoza, like Saxenda, is merely a brand name for the drug liraglutide, and Zepbound, like Mounjaro, is merely a brand name for the drug tirzepatide. (*See id.*) Because Saxenda and Mounjaro are part of this MDL, Victoza and Zepbound are as well.

suggested that this number will increase (*see* June 10, 2024 Hr’g Tr. at 16:18–23 (“And there are known to us, meaning co-lead counsel, approximately 5,000 Novo-only cases under investigation; about 1,200 Lilly-only cases; and then about 1,400 combined Novo and Lilly.”); Feb. 24, 2025 Hr’g Tr. at 8:1–12 (cautiously asserting that “I don’t think we see anything that would expect the prediction to change”); *but see* July 29, 2025 Hr’g Tr. at 49:11–18 (“[I]n Morgan & Morgan’s view, I don’t think there will be 10,000 cases in the MDL.”)). Although the alleged drug, dosage, and precise injury vary by Plaintiff, there are many commonalities. Notably, each Plaintiff claims they were prescribed one or more of the eight identified medications for the treatment of type 2 diabetes and/or chronic weight management and that as a result, they suffered gastrointestinal symptoms and/or injuries, such as “debilitating cyclical vomiting,” gastroparesis, ileus, intestinal obstruction, gallbladder injury, vitamin deficiency, Wernicke’s Encephalopathy, ischemic bowel, and necrotizing pancreatitis. (Doc. No. 294 at ¶¶ 4, 13, 41.)

Although the Master Complaint references numerous diagnoses and symptoms, Plaintiffs’ counsel have represented that they anticipate the “vast majority, over 95%” of the cases eventually filed as part of this MDL will allege that the Plaintiff suffered or continues to suffer from gastroparesis. (*See* June 10, 2024 Hr’g Tr. at 17:23–25.) Thus, the Court found it pertinent to frontload resolution of the parties’ debate about when a diagnosis of gastroparesis will be considered reliable, and in particular, whether a diagnosing physician can reliably make such a diagnosis without performing a gastric emptying study. (*See* Doc. No. 235 at 3–5.)

#### **A. Gastroparesis Overview**

The extensive briefing and dozens of exhibits filed in connection with the parties’ motions give rise to one unavoidable fact: The stomach is a complex organ. Although it lies

dormant in times of fasting, when we eat, an interrelated system of gut hormones, pacemaker cells, muscles, and valves work in tandem to store, mix, grind, and propel liquids and solids from the stomach into the duodenum.<sup>4</sup> A. Patrick & O. Epstein, *Review Article: Gastroparesis*, 27 *Alimentary Pharmacology & Therapeutics* 724, 724–40 (2008) (filed as Doc. No. 359-3, Ex. F) (discussing normal gastric function).

Gastroparesis is a disorder that affects this normal functioning and is one of the two most common sensorimotor disorders of the upper gastrointestinal (“GI”) tract. Beom Jin Kim & Braden Kuo, *Gastroparesis and Functional Dyspepsia: A Blurring Distinction of Pathophysiology and Treatment*, 25 *J. Neurogastroenterology & Motility* 27, 27 (2019) (filed as Doc. No. 359-3 at Ex. H) (“*Blurring*”) (“The most common sensorimotor disorders involving the upper gastrointestinal tract are gastroparesis (GP) and functional dyspepsia (FD).”). The term “gastroparesis” literally means paralysis of the stomach, and it occurs when a patient’s stomach, regardless of the underlying cause, does not normally move solid foods through the digestive tract. (May 14, 2025 Pt. 1 Tr. at 11:17–22 (Dr. Raines testifying that in “patients with gastroparesis, their stomach is not pushing normally”).)

Gastroparesis is characterized by upper GI symptoms, such as nausea, vomiting, early satiety,<sup>5</sup> and abdominal pain, and delayed gastric emptying in the absence of a mechanical obstruction. Michael Camilleri et al., *ACG Clinical Guideline: Gastroparesis*, 117 *The Am. J. of Gastroenterology* 1197, 1197 (2022) (filed as Doc. No. 360-4) (the “2022 ACG Guideline”).<sup>6</sup>

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<sup>4</sup> The duodenum is the first segment of the small intestine. *Duodenum*, Oxford English Dictionary, [https://www.oed.com/dictionary/duodenum\\_n?tl=true](https://www.oed.com/dictionary/duodenum_n?tl=true) (last visited Aug. 6, 2025).

<sup>5</sup> “Satiety” refers to feelings of fullness, and “early satiety” refers to the “inability to finish a standard meal.” (Raines Dep. Tr. at 84:16–22.)

<sup>6</sup> See also, e.g., Jolien Schol et al., *Rome Foundation and Int’l Neurogastroenterology and Motility Societies’ Consensus on Idiopathic Gastroparesis*, 10 *The Lancet Gastroenterology & Hepatology* 68, 68 (2025) (filed as Doc. No. 360-7) (the “2025 Rome Consensus”) (“Historically,

Because gastroparesis has multiple potential causes or origins, it is often divided into subsets based on etiology and pathophysiology. Michael Camilleri et al., *What are the Important Subsets of Gastroparesis?*, 24 *Neurogastroenterology & Motility* 597, 597 (2012) (filed as Doc. No. 359-3, Ex. I) (“*Subsets 2012*”); (see also Doc. No. 360-9 at 62:18–22 (“Raines Dep. Tr.”) (discussing subtypes of gastroparesis)). The most common subsets are diabetic<sup>7</sup> and idiopathic<sup>8</sup> gastroparesis. (May 14, 2025 Pt. 1 Tr. at 81:12–18 (Dr. Raines testifying that these subsets cover the “typical patient”).) But here, the Court is concerned with a third subset: iatrogenic gastroparesis. See *Subsets 2012* at 598.

Iatrogenic gastroparesis refers to gastroparesis caused by medical intervention. (Raines Dep. Tr. at 64:5–8.) The most common iatrogenic cause is surgery that results in injury to the vagus nerve, but medications known to cause delayed gastric emptying, like opiates and GLP-1 RAs, may also lead to drug-induced gastroparesis. *Subsets 2012* at 598. Drug-induced gastroparesis is different from the other subsets of gastroparesis in that it is temporary and

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gastroparesis has been defined as a condition characterized by upper gastrointestinal symptoms and notably delayed gastric emptying in the absence of any mechanical obstruction.”); Jolien Schol et al., *United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) Consensus on Gastroparesis*, 9 *United European Gastroenterology J.* 287, 288 (2021) (filed as Doc. No. 360-13) (the “*2020 UEG & ESNM Consensus*”) (“Gastroparesis is a condition characterized by epigastric symptoms (nausea, vomiting, postprandial fullness, early satiation, and epigastric pain) and significantly delayed gastric emptying (GE) rate in the absence of any mechanical obstruction.”); Michael Camilleri, MD, et al., *Clinical Guideline: Mgmt. of Gastroparesis*, 108 *The Am. J. of Gastroenterology* 18, 19 (2013) (filed as Doc. No. 360-5) (the “*2013 ACG Guideline*”) (“Gastroparesis is defined as a syndrome of objectively delayed gastric emptying in the absence of mechanical obstruction and cardinal symptoms including early satiety, postprandial fullness, nausea, vomiting, bloating, and upper abdominal pain.”).

<sup>7</sup> Diabetic gastroparesis is typically the result of damage to the vagus nerve or loss of the Interstitial Cells of Cajal (“ICC”), and complications of Type 2 diabetes is the most common cause of gastroparesis. *Subsets 2012* at 598; (see also May 14, 2025 Pt. 1 Tr. at 14:3–6 (Dr. Raines discussing epidemiological study); *id.* at 247:22–248:1 (Dr. Raines confirming that “in patients with diabetic gastroparesis, there is permanent injury to the nerves and muscles of the stomach, resulting from persistently elevated blood sugar levels”)).

<sup>8</sup> Idiopathic gastroparesis refers to gastroparesis of unclear origin. *Idiopathic*, Cambridge Dictionary, <https://dictionary.cambridge.org/dictionary/english/idiopathic> (last visited Aug. 6, 2025).

should cease when the patient stops taking the medication at issue. By contrast, other forms of gastroparesis tend to be chronic, or lifelong, conditions, often having been caused by irreversible damage to the nerves and/or mechanics of the stomach.

The parties and the experts agree that when diagnosing all subsets of gastroparesis other than drug-induced gastroparesis, three requirements must be satisfied. First, the patient must exhibit upper GI symptoms. Nausea and vomiting are considered the cardinal symptoms of gastroparesis, but early satiation and postprandial fullness<sup>9</sup> are also associated with the disorder. *2025 Rome Consensus* at 68–69; Benjamin Stein, MD, et al., *Gastroparesis: A Review of Current Diagnosis & Treatment Options*, 49 J. Clinical Gastroenterology 550, 550–51 (2015) (filed as Doc. No. 359-3 at Ex. J) (“GP: *Diagnosis & Treatment*”) (“The diagnosis of GP requires the presence of symptoms compatible with delayed gastric emptying . . .”). Bloating and abdominal pain are also considered possible symptoms. All of these symptoms are nonspecific, meaning they overlap with the symptoms of many other disorders, including centrally mediated nausea, functional dyspepsia, cyclic vomiting syndrome, and peptic ulcer.

Second, the physician must confirm that the symptoms are not being caused by a gastric outlet obstruction or other mechanical factor (e.g., an ulcer, tumor, bezoar). *2025 Rome Consensus* at 70. The absence of obstruction is typically confirmed through an upper endoscopy. *Id.*; *2022 ACG Guideline* at 1197 (explaining that “mechanical obstruction . . . should be excluded by imaging studies such as upper gastrointestinal endoscopy or radiology”);

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<sup>9</sup> Postprandial fullness, like early satiety, refers to feelings of fullness that accompany eating. Postprandial fullness is typically associated with impaired distal gastric (antral) function, while early satiety is due to impaired proximal gastric (fundic function). H.P. Parkman et al., *Early Satiety and Postprandial Fullness in Gastroparesis Correlate with Gastroparesis Severity, Gastric Emptying, and Water Load Testing*, 29 Neurogastroenterology & Motility 1, 2 (2016), <https://onlinelibrary.wiley.com/doi/10.1111/nmo.12981> (filed as Doc. No. 377-16).

*GP: Diagnosis & Treatment* at 551–52 (explaining that the absence of a mechanical obstruction is “established with upper endoscopy” and is “imperative in all patients with suspected GP”).

Last, there must be objective evidence of delayed gastric emptying. *See 2025 Rome Consensus* at 70 (“As symptoms of gastroparesis lack specificity, a demonstration of delayed gastric emptying is necessary for diagnosis.”); *see also, e.g., 2022 ACG Guideline* at 1197 (“Gastroparesis (GP) is a motility disorder characterized by symptoms and *objective documentation* of delayed gastric emptying (GE) of solid food without mechanical obstruction . . .” (emphasis added)). Gastric emptying scintigraphy is recognized as the “gold standard” test for measuring gastric emptying. *See, e.g., 2022 ACG Guideline* at 1200; *GP: Diagnosis & Treatment* at 552 (“Scintigraphy is considered the gold standard to establish the diagnosis of GP.”). In this test, the patient ingests a standard, radiolabeled meal, and the physician monitors its digestion at various intervals between 1 and 4 hours. *See, e.g., GP: Diagnosis & Treatment* at 552; (*see also* May 14, 2025 Pt 2 Tr. at 13:9–18 (Dr. Siegel discussing scintigraphy tests)). Gastric emptying breath test and the use of a wireless motility capsule (“WMC”) are also broadly accepted as appropriate methods for measuring emptying rates. *See, e.g., GP: Diagnosis & Treatment* at 552–53.

Again, there is no dispute that all three requirements—symptoms, absence of obstruction, and delayed emptying documented with a gastric emptying study—must be met before a physician can reliably diagnose gastroparesis in all subsets of the disorder except for drug-induced gastroparesis. (*See* May 16, 2025 Hr’g Tr. at 15:3–12 (Plaintiffs’ counsel agreeing that “permanent gastroparesis as a diagnosis” requires a gastric emptying study); July 29, 2025 Hr’g Tr. at 13:15–23 (“Mr. Buxner: . . . Like both experts agreed, Dr. Raines and Dr. Nguyen, if a patient is pulled from the GLP-1 RA . . . and the symptoms persist, then a GES

would be ordered to see what is going on. The Court: Okay. And you agree with that? Mr. Buxner: Oh I agree with that.”.) When it comes to drug-induced gastroparesis, however, the experts disagree about whether a physician can reliably diagnose a patient in the absence of objective testing of delayed gastric emptying, and to the extent some testing occurs, which categories of evidence constitute “objective documentation” of delayed emptying. The Court discusses the opinions of Dr. Raines, Dr. Siegel, and Dr. Nguyen on this issue in turn.

### **B. Dr. Raines’s Report**

Plaintiffs’ first expert is Dr. Raines. Dr. Raines is the Chief of Gastroenterology and Professor of Clinical Medicine for the Louisiana State University Health Sciences Center. (Doc. No. 359-3, Ex. B, “Raines Rpt.” at 2.) In that role, his responsibilities are split between “patient care, medical education, and clinical research.” (*Id.*) Dr. Raines estimates that he has seen around 2,000 patients per year during his 18-year career, the majority of whom were referred by other gastroenterologists for further evaluation of complex cases or rare diseases, including patients previously diagnosed with gastroparesis. (*Id.*)

Dr. Raines opines that a physician can use the “differential diagnosis” method to reliably diagnose drug-induced gastroparesis without objective testing to show a lack of mechanical obstruction or delayed gastric emptying. (*Id.* at 7.) Dr. Raines summarizes this method in his report:

Medical evaluations begin with a detailed history and physical examination. This information is used to develop a list of potential diagnoses, or ‘differential diagnoses,’ which may explain a patient’s symptoms. These diagnoses are typically organized by likelihood then reordered or excluded based upon evidence accumulated through diagnostic testing, clinical course, and response to therapy. A final diagnosis is made by the treating physician based upon their judgment of which diagnosis is most likely. Although some medical diagnoses rely more heavily upon



clinical history, exam findings, or testing results, they are rarely made by a single piece of evidence.

(*Id.* at 6–7.) Dr. Raines explains that for a patient presenting with chronic nausea and vomiting (i.e., nausea and vomiting for more than seven days), his differential diagnosis considers numerous pathologies, including gastroparesis; organic pathologies (including peptic ulcer disease, gastric cancer, gallstone disease, and pancreatitis); functional disorders (including functional dyspepsia, chronic nausea and vomiting syndrome, cyclic vomiting syndrome, and cannabinoid hyperemesis syndrome); and psychiatric disorders (including anorexia and bulimia). (*Id.* at 7–8; *see also* Raines Dep. Tr. at 85:8–112:10 (discussing differential diagnosis).) Various information may lead Dr. Raines to “rule out” these pathologies. For example, he considers “vomiting of undigested food” to be “pathognomonic<sup>10</sup> for delay in gastric emptying if the food was ingested >4 hours prior,” and thus, indicative of gastroparesis. (Raines Rpt. at 7.) Likewise, “[i]n cases in which the onset of symptoms correlates with initiation of a drug known to induce delay in gastric emptying, a diagnosis of drug-induced gastroparesis is more likely.” (*Id.*) By contrast, symptoms of “recurrent pain in the right upper abdomen which occurs within 30–60 minutes following a meal” is indicative of gallbladder disease. (*Id.*) And where the patient has a history of childhood abuse or trauma, functional disorders may be more likely. (*Id.* at 7–8.)

Under this framework, Dr. Raines notes that a history and physical examination alone can be sufficient for a physician to diagnose drug-induced gastroparesis. (*Id.* at 8; *see also* Raines Dep. Tr. at 107:9–12.) He acknowledges, however, that imaging of the abdomen by computerized tomography (CT or CAT) scan or magnetic resonance imaging (MRI) may also

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<sup>10</sup> “Pathognomonic means [it’s] a clear indicator. It’s kind of difficult to dispute.” (Raines Dep. Tr. at 101:19–102:10.)

“be useful in evaluating for mechanical obstruction of the gastrointestinal tract” and such tests could reveal other pathologies including peptic ulcer disease, gastric cancer, pancreatitis, or gallbladder disease. (Raines Rpt. at 10.) Likewise, “[i]maging study findings which support a diagnosis of gastroparesis include gastric distension and/or retained gastric food.” (*Id.*) Dr. Raines considers “[t]he discovery of retained gastric food (RGF) on upper endoscopy [to be] highly suggestive of delayed gastric emptying.” (*Id.*; *see also id.* at 12.) Finally, Dr. Raines concedes that gastric emptying scintigraphy is the “test most commonly used to evaluate delay in gastric emptying,” and that gastric emptying breath test and WMC also provide reliable data on the rate of gastric emptying. (*Id.* at 10–11.) Although helpful, he maintains that none of these tests are necessary for a physician to reach a reliable diagnosis for drug-induced gastroparesis.

Instead, when a “patient’s history and physical exam are consistent with a diagnosis of drug-induced gastroparesis and negative for evidence of alternative diagnoses,” Dr. Raines “assign[s] a diagnosis of drug-induced gastroparesis.” (*Id.* at 12.) He then directs the patient to stop taking the offending drug. (*Id.*) “A diagnosis of drug-induced gastroparesis may be further supported in patients who experience resolution of symptoms after medication withdrawal.” (*Id.*; *see also id.* at 14 (“Improvement in symptoms following withdrawal of an offending drug supports a diagnosis of drug-induced gastroparesis and obviates the need for additional testing.”).) Dr. Raines believes the resolution of symptoms also indicates the lack of mechanical obstruction, which, again, he does not rule out *before* assigning a diagnosis of drug-induced gastroparesis. (*Id.* at 12.) When, however, the symptoms persist, Dr. Raines agrees that “further imaging and/or upper endoscopy followed by formal measurement of gastric emptying by [scintigraphy], [breath test], or WMC” is needed. (*Id.*)

At the end of his report, Dr. Raines summarizes his opinion as containing seven conclusions:

1. Gastroparesis is a clinical diagnosis defined by symptomatic delay in emptying of the stomach due to abnormal gastric motility.
2. Drug-induced gastroparesis is a subtype of gastroparesis which accounts for an estimated 11.8% to 22% of all cases of gastroparesis in the United States.
3. In cases of drug-induced gastroparesis, withdrawal of the offending drug is recommended as the first step in management.
4. Drug-induced gastroparesis may be diagnosed in the absence of a [gastric emptying scintigraphy] study.
5. A diagnosis of drug-induced gastroparesis may be supported by imaging studies, including plain x-ray, CT scan, MRI and/or abdominal ultrasound.
6. A positive [scintigraphy study, i.e., a study that reveals significantly delayed emptying rates,] may also support a diagnosis of drug-induced gastroparesis.
7. Patients with symptoms of gastroparesis who fail to improve following drug withdrawal require additional testing including upper endoscopy, imaging, and/or [scintigraphy].

(*Id.* at 14.)

### **C. Dr. Siegel's Report**

Plaintiffs' second expert is Dr. Siegel. Unlike Dr. Raines, Dr. Siegel is not a gastroenterologist. Instead, he is a radiologist with a certification of special competence in Nuclear Medicine and more than 37 years of experience in diagnostic imaging. (Doc. No. 395-3, Ex. C, "Siegel Rpt." at 3.) During that time, he served as the Chief of Diagnostic Radiology and Nuclear Medicine for the VA Maryland Healthcare System and as a professor at the University of Maryland. (*Id.*) Dr. Siegel has interpreted the results from tens of thousands of

nuclear medicine examinations, including around 2,000 gastric emptying scintigraphy studies, in addition to CT scans, MRIs, and other imaging studies. (May 14, 2025 Pt 2 Tr. at 12:18–13:1.) He has also interpreted the presence or absence of mechanical obstruction via CT scans and upper GI imaging on thousands of occasions and reported the presence of retained food and gastric distension, gastric wall thickening, and gastric masses on CT scans in thousands of cases. (Siegel Rpt. at 5.) In addition to performing and reviewing the results of these various nuclear medicine and imaging tests, Dr. Siegel has also personally diagnosed gastroparesis on at least 100 occasions. (*Id.*)

Dr. Siegel’s report includes a detailed overview of the anatomy of the stomach, the normal gastric emptying process, GLP-1 RAs’ potential effects on gastric emptying, and the condition known as gastroparesis. (*Id.* at 5–10.) As relevant here, Dr. Siegel explains that gastroparesis is a “condition characterized by abnormal gastric motility with delayed gastric emptying in the absence of a mechanical . . . outlet obstruction.” (*Id.* at 10.) He also recognizes that gastroparesis is “defined by three elements:” “[1] being associated with gastrointestinal symptoms . . . ; [2] occurring in the absence of a mechanical obstruction of the pylorus; and [3] occurring in the presence of delayed gastric emptying.” (*Id.* at 10.)

Like Dr. Raines, Dr. Siegel opines that the differential diagnosis method is the appropriate method for diagnosing a patient with drug-induced gastroparesis. (*Id.* at 11.) He identifies “patient history and physical exam” as the “starting point.” (*Id.*) “The steps taken beyond patient history and physical exam” will, however, “vary based on the specific circumstances of th[e particular] patient.” (*Id.*) In particular, the testing that the physician orders will depend on which diagnoses the presenting physician thinks are most likely given the patient history and the results of the physical exam. (*Id.* at 12, 14.) Dr. Siegel identifies

multiple tests which may be of use in diagnosing gastroparesis, including “computed tomography (CT), ultrasound, conventional x-ray studies, upper GI series, esophagogastroduodenoscopy (EGD), magnetic resonance imaging (MRI), and nuclear medicine gastric emptying studies, also known as gastric emptying scintigraphy.” (*Id.* at 12; *see also id.* at 12–14, 18–24 (discussing various imaging studies).) Dr. Siegel emphasizes that regardless of the tests conducted, “it is important to consider and rule out a variety of alternative diagnoses before concluding that a patient does indeed have gastroparesis” especially because “the symptoms of gastroparesis are nonspecific and overlap to a greater or lesser degree with many conditions.” (*Id.* at 15.)

Like Dr. Raines, Dr. Siegel also opines that when “gastroparesis is based on a permanent (or unknown) underlying condition, it should be confirmed by [gastric emptying study] and upper endoscopy.” (*Id.* at 16.) He emphasizes that “[b]ecause [gastroparesis] can be difficult to distinguish from other conditions, especially functional dyspepsia, it is important to use confirmatory diagnostic testing.” (*Id.*) These concerns fall away, however, when the physician confronts drug-induced gastroparesis, which, according to Dr. Siegel, “has features that are likely to be obvious from history and physical examination.” (*Id.*) Notably, in addition to having symptoms associated with delayed gastric emptying, GI complaints will “only begin after the drug is started and begins to induce delayed gastric emptying.” (*Id.*) If symptoms improve once the drug is withdrawn, it is further evidence that “the gastric emptying effect of the drug is responsible for the patient’s symptoms.” (*Id.* at 16–17.) If, however, symptoms persist after the patient is taken off the medication, then Dr. Siegel would “consider a nuclear medicine gastric emptying study.” (*Id.* at 17–18.)

At the end of his report, Dr. Siegel summarizes his opinion as including three conclusions:

1. GLP-1 RA-induced gastroparesis can be diagnosed based on patient history, differential diagnosis, current symptoms, and physical exam.
2. Imaging endoscopy, or a [gastric emptying scintigraphy study], can provide an additional datapoint for diagnosis of GLP-1 RA-induced gastroparesis but is usually not necessary. This should be done in a personalized, patient-specific manner rather than a ‘one size fits all’ approach.
3. A [gastric emptying scintigraphy study] is not required to diagnose GLP-1 RA-induced gastroparesis.

(*Id.* at 25.)

#### **D. Dr. Nguyen’s Report**

That leaves Defendants’ expert, Dr. Nguyen. Dr. Nguyen is the Clinical Professor of Medicine at Stanford University and Interim Chief of Gastroenterology and Hepatology. (Doc. No. 359-3, Ex. D, “Nguyen Rpt.” at 1.) She graduated from the UCLA School of Medicine and after graduation, completed a GI fellowship at the California Pacific Medical Center in San Francisco, where her research focused on gastroparesis. (*Id.*) She has published more than 90 peer-reviewed original research papers, review articles, and 8 book chapters, all of which focus predominantly on gastroparesis and gastroparesis-like disorders. (*Id.*) She is also a content expert coauthor of the *2022 ACG Guideline* and contributed to the *2025 Rome Consensus*. (*Id.*) In addition to her research and publishing work, Dr. Nguyen has cared for thousands of patients with gastroparesis or gastroparesis-like symptoms during her 19-year career. (*Id.*)

Dr. Nguyen disagrees with Drs. Raines and Siegels’ opinion that drug-induced gastroparesis can be diagnosed based purely on the results of a patient history and physical examination. Indeed, Dr. Nguyen states that “[d]ue to the non-specific nature of gastroparesis

symptoms and the high error rate of symptom-based approaches . . . , a diagnosis of gastroparesis cannot be made based on clinical presentation alone.” (*Id.* at 8.) Instead, she opines that to reliably diagnose *any* subset of gastroparesis, including drug-induced gastroparesis, “three criteria have to be met: (1) symptoms consistent with gastroparesis; (2) exclusion of mechanical obstruction with esophagogastroduodenoscopy (EGD) or a radiographic study; and (3) objective evidence of delayed gastric emptying of solids.” (*Id.*) For the third requirement, only three gastric emptying tests, “when properly performed, are accepted for use in the diagnosis of [gastroparesis]: gastric emptying scintigraphy[,] the stable isotope gastric-emptying breath test,” and the “wireless capsule motility (WCM) test (SmartPill).”<sup>11</sup> (*Id.*)

Dr. Nguyen emphasizes that her opinion is consistent with all the domestic and international medical guidelines on diagnosing and treating gastroparesis. (*Id.* at 8–13.) And she states she “will not make a diagnosis of gastroparesis in a patient without first ruling out mechanical obstruction, either with an EGD or other radiographic techniques,” nor will she make a diagnosis “without a gastric emptying study (typically scintigraphy).” (*Id.* at 15.) Indeed, Dr. Nguyen’s own practice “often involves ‘un-diagnosing’ patients” who have been wrongly diagnosed with gastroparesis without objective testing, and some days she “spend[s] more time correcting prior misdiagnoses of gastroparesis than [she does] diagnosing gastroparesis.” (*Id.*)

In addition to her affirmative opinions, Dr. Nguyen also issues four opinions in response to the reports of Drs. Raines and Siegel. (*Id.* at 16–18.) First, she acknowledges that “certain

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<sup>11</sup> Dr. Nguyen notes that WMC, which was approved by the FDA in 2006, has been out of production since 2023, leaving only scintigraphy and breath test as the currently available, accepted methods for measuring gastric emptying. (Nguyen Rpt. at 8.)

medications (including GLP-1 RAs) can transiently delay gastric emptying resulting in symptoms that mimic (but are not equivalent to) the medical condition known as gastroparesis and that resolve upon treatment cessation.” (*Id.* at 16.) She differentiates this transient condition from the “chronic disease” of gastroparesis. (*Id.*) Second, she disputes that resolution of GI symptoms after stopping a medication is evidence that the patient had delayed gastric emptying. (*Id.* at 17.) Instead, this “may confirm, at most, that a patient had a GI side effect of the medication.” (*Id.*) Third, she opines that although GI symptoms are common with the use of GLP-1 RAs, delayed gastric emptying is relatively rare, as demonstrated by the preliminary results of a study conducted by Camille Lupianez-Merly. (*Id.*) Finally, Dr. Nguyen acknowledges that although scintigraphy can only show the rate of emptying on a single day, it remains the “most reliable method available to assess gastric emptying” and either it or another approved gastric emptying test is “required to make a reliable diagnosis of gastroparesis.” (*Id.* at 17–18.)

#### **E. Motions to Exclude**

Defendants have moved for exclusion of the opinions of Drs. Raines and Siegel, and Plaintiffs have moved for partial exclusion of Dr. Nguyen’s opinions. On May 14, 2025, the Court held an evidentiary hearing, during which all three physicians testified. And on May 19, 2025, the parties provided oral argument on the various motions. On July 23, 2025, Plaintiffs moved to supplement the record to include a document that Lilly submitted to the FDA in October 2023, arguing that statements made within that document estop Lilly from arguing certain positions in this litigation. The Court addresses the motions to exclude before turning to the motion to supplement and the additional document’s effect, if any, on the Court’s ruling.



## II. MOTIONS TO EXCLUDE

### A. Legal Standard

Federal Rule of Evidence 702 outlines the conditions that must be met for a witness to testify as an expert:

A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if the proponent demonstrates to the court that it is more likely than not that:

(a) the expert’s scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;

(b) the testimony is based on sufficient facts or data;

(c) the testimony is the product of reliable principles and methods; and

(d) the expert’s opinion reflects a reliable application of the principles and methods to the facts of the case.

Fed. R. Evid. 702. This rule requires the trial judge to act as a “gatekeeper,” ensuring that “any and all expert testimony or evidence is not only relevant, but also reliable.” *Pineda v. Ford Motor Co.*, 520 F.3d 237, 243 (3d Cir. 2008) (cleaned up); *see also Sikkelee v. Precision Airmotive Corp.*, No. 4:07-CV-00886, 2021 WL 392101, at \*2 (M.D. Pa. Feb. 4, 2021) (“A district court exercises more control over experts than over lay witnesses,” because “expert evidence can be both powerful and quite misleading” given “the difficulty in evaluating it.” (quotation marks omitted)). “*Daubert*’s general holding—setting forth the trial judge’s general ‘gatekeeping’ obligation—applies not only to testimony based on ‘scientific’ knowledge, but also to testimony based on ‘technical’ and ‘other specialized’ knowledge.” *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 141 (1999).

To be admissible under Rule 702, expert testimony must satisfy “three major

requirements: (1) the proffered witness must be an expert, *i.e.*, must be qualified; (2) the expert must testify about matters requiring scientific, technical or specialized knowledge; and (3) the expert's testimony must assist the trier of fact." *Pineda*, 520 F.3d at 244. These factors are often referred to as "qualification," "reliability," and "fit." *See Schneider ex rel. Estate of Schneider v. Fried*, 320 F.3d 396, 404 (3d Cir. 2003) ("We have explained that Rule 702 embodies a trilogy of restrictions on expert testimony: qualification, reliability, and fit.").

"Qualification requires that the witness possess specialized expertise." *Pineda*, 520 F.3d at 244 (cleaned up). The Third Circuit has counseled that "a broad range of knowledge, skills, and training qualify an expert." *Id.*; *accord Schneider ex rel. Schneider*, 320 F.3d at 404; *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 741 (3d Cir. 1994). Under the reliability prong, an "expert's testimony is admissible so long as the process or technique the expert used in forming the opinion is reliable." *Pineda*, 520 F.3d at 247 (quoting *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d at 742). In other words, the proffered testimony "must be based on the methods and procedures of science rather than on subjective belief or unsupported speculation" and the "expert must have good grounds for his or her belief." *Schneider ex rel. Schneider*, 320 F.3d at 404 (cleaned up). The Third Circuit has identified eight factors that may be relevant to the reliability analysis:

(1) whether a method consists of a testable hypothesis; (2) whether the method has been subject to peer review; (3) the known or potential rate of error; (4) the existence and maintenance of standards controlling the technique's operation; (5) whether the method is generally accepted; (6) the relationship of the technique to methods which have been established to be reliable; (7) the qualifications of the expert witness testifying based on the methodology; and (8) the non-judicial uses to which the method has been put.

*In re Paoli*, 35 F.3d at 742 n.8. Last, the “expert testimony must fit the issues in the case,” meaning the “expert’s testimony must be relevant for the purposes of the case and must assist the trier of fact.” *Id.*; *see also Daubert v. Merrell Down Pharms., Inc.*, 509 U.S. 579, 591 (1993) (“Fit is not always obvious, and scientific validity for one purpose is not necessarily scientific validity for other, unrelated purposes.”).

The party proposing the expert witness must show that each prong—qualification, reliability, and fit—is satisfied by a preponderance of proof. *Oddi v. Ford Motor Co.*, 234 F.3d 136, 144 (3d Cir. 2000); *see also In re Paoli*, 35 F.3d at 743 & 744 n.11 (explaining that the proponent must make more than a *prima facie* showing that a technique is reliable); *Ellison v. United States*, 753 F. Supp. 2d 468, 476 (E.D. Pa. 2010) (“The burden is on the proponent of the evidence—here the plaintiff—to establish admissibility by a preponderance of the evidence.”). However, at all times, we must remember that the Rules of Evidence generally “embody a strong preference for admitting any evidence that may assist the trier of fact,” and Rule 702 specifically has a “liberal standard of admissibility.” *United States v. Downing*, 753 F.2d 1224, 1230 (3d Cir. 1985); *see also Oddi*, 234 F.3d at 156 (“The test is not whether the expert might have done a better job.” (cleaned up)).

With this standard in mind, the Court addresses the motions to exclude the opinions of Dr. Raines, Dr. Siegel, and Dr. Nguyen in turn.

## **B. Dr. Raines**

Defendants move to exclude as unreliable Dr. Raines’s opinion that a physician can diagnose drug-induced gastroparesis without performing one of the three recognized gastric emptying studies (i.e., scintigraphy, breath test, or WMC). (Doc. No. 360-1 at 16–22, 24–26; Doc. No. 361-1 at 18–25.) Plaintiffs counter that Dr. Raines’s opinion is reliable because he

employs a differential diagnosis, which is accepted by the Third Circuit and the medical community as a reliable methodology for the assessment and diagnosis of patients. (Doc. No. 379 at 28–42.)

The phrase “differential diagnosis” refers to the method by which a physician uses some combination of the findings of a physical examination, medical history, and clinical tests to reach a conclusion about a patient’s illness and/or its cause.<sup>12</sup> See *Kannankeril*, 128 F.3d at 807; see also *Magistrini*, 180 F. Supp. 2d at 609 (“A reliable differential diagnosis typically is performed after physical examinations, the taking of medical histories, and the review of clinical tests, including laboratory tests, and generally is accomplished by determining the possible causes for the patient’s symptoms and then eliminating each of these potential causes until reaching one that cannot be ruled out, or determining which of those that cannot be excluded is the most likely.” (quotation marks omitted)).

Plaintiffs are correct that the Third Circuit “generally recognizes differential diagnosis as a reliable methodology” when “properly performed.” *Feit v. Great W. Life & Annuity Ins. Co.*, 271 F. App’x 246, 254 (3d Cir. 2008) (citing *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 156 (3d

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<sup>12</sup> As Plaintiffs note, there is a difference between differential diagnosis, which refers to assigning a patient a particular diagnosis (e.g., lung cancer), and differential etiology, which refers to identifying the cause of the patient’s illness (e.g., long term cigarette use). (See May 19, 2025 Hr’g Tr. at 42:6–43:19.) Courts often use the phrase “differential diagnosis” when “differential etiology” would be more appropriate. Nevertheless, this Court finds the case law on “differential etiology” persuasive in cases, like the one here, where a physician is assigning a specific diagnosis based on a patient’s symptoms. Notably, in both scenarios, the physician is tasked with determining which option among many is giving rise to a plaintiff’s symptoms by systematically including and excluding various possibilities. Compare *Kannankeril v. Terminix Intern., Inc.*, 128 F.3d 802, 807 (3d Cir. 1997) (“Differential diagnosis is defined for physicians as ‘the determination of which of two or more diseases with similar symptoms is the one from which the patient is suffering, by a systematic comparison and contrasting of the clinical findings.’” (quoting *Stedman’s Med. Dictionary* 428 (25th ed. 1990))), with *Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F. Supp. 2d 584, 609 (D.N.J. 2002) (“Differential diagnosis, or differential etiology, is a standard scientific technique which identifies the cause of a medical problem by eliminating the likely causes until the most probable one is isolated.”).

Cir. 1999) and *In re Paoli*, 35 F.3d at 758); *see also Ellison v. United States*, 753 F. Supp. 2d 468 (E.D. Pa. 2010) (“The Third Circuit repeatedly has recognized differential diagnosis as a reliable methodology when appropriately performed.”); *Magistrini*, 180 F. Supp. 2d at 609 (“In this Circuit, the technique of differential diagnosis has been found to be a reliable technique when properly performed.”). But “the mere statement by an expert that he or she applied differential diagnosis in determining causation does not ipso facto make that application scientifically reliable or admissible.” *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 551 (W.D. Pa. 2003). Instead, “such a methodology must be properly supported in order to be reliable and admissible.” *Feit v. Great W. Life & Annuity Ins. Co.*, 460 F. Supp. 2d 632, 644 (D.N.J. 2006).

“A physician need not conduct every possible test to rule out all possible causes of a patient’s illness, ‘so long as he or she employed sufficient diagnostic techniques to have good grounds for his or her conclusion.’” *Heller*, 167 F.3d at 156 (quoting *In re Paoli*, 35 F.3d at 761); *accord Kannankeril*, 128 F.3d at 807. A physician’s differential diagnosis may be found unreliable when: (1) the physician has “engaged in very few standard diagnostic techniques by which doctors normally rule out alternative causes *and* the doctor offer[s] no good explanation as to why his or her conclusion remain[s] reliable,” or (2) the defendant has “pointed to some likely [alternative] cause of the plaintiff’s illness” and the physician has failed to offer “a good explanation as to why their conclusion remain[s] reliable.” *In re Paoli*, 35 F.3d at 760–62; *accord Kannankeril*, 128 F.3d at 808.

Here, Defendants argue that Dr. Raines’s opinion should be excluded because his method rejects the standard diagnostic techniques used by physicians diagnosing all forms of gastroparesis, rests on unsupported assumptions, and fails to adequately account for likely

alternative diagnoses for a patient’s symptoms. (Doc. No. 360-1 at 17–22, 24–26; Doc. No. 361-1 at 17–25.) The Court begins by outlining the techniques underlying Dr. Raines’s proposed differential diagnosis. We then consider whether his methodology is contrary to the existing medical consensus for diagnosing gastroparesis, including drug-induced gastroparesis. Finding that it is inconsistent with the established standards in the medical community, the Court considers whether Dr. Raines has offered a “good explanation as to why” his method nevertheless allows a physician to reliably find that drug-induced gastroparesis is the most likely diagnosis when certain criteria are satisfied.

#### 1. Dr. Raines’s Differential Diagnosis

As noted previously, Dr. Raines does not dispute that all three requirements—symptoms, absence of obstruction, and delayed emptying *confirmed* by a gastric emptying study—must be met before a physician can reliably diagnose gastroparesis in all subsets of the disorder except for drug-induced gastroparesis. (See Raines Rpt. at 13; May 14, 2025 Pt. 1 Tr. at 107:22–112:6.) And although Dr. Raines’s testimony was somewhat inconsistent during both his deposition and the evidentiary hearing, he ultimately concluded that the same three broad requirements—symptoms, absence of obstruction, and delayed emptying—must be satisfied for a physician to reliably diagnose a patient with drug-induced gastroparesis. (See May 14, 2025 Pt. 1 Tr. at 13:11–13, 123:12–16, 124:17–125:9.) In the drug-induced context, however, Dr. Raines departs in his opinion as to how these broad requirements are satisfied, opining that a physician can find all the requirements satisfied based only on the results of a physical examination and patient’s medical history, and *without* performing either (1) an endoscopy to confirm absence of obstruction or (2) a gastric emptying study or other objective testing to confirm delayed gastric emptying. (See *id.* at 54:6–11, 56:11–22.)

During the evidentiary hearing, Dr. Raines outlined his proposed differential diagnosis, explaining how a physician “rules in” a diagnosis of gastroparesis and “rules out” other potential diagnoses without objective testing. (*Id.* at 12:22–13:5; *id.* at 21:22–47:16 (discussing each step of differential diagnosis).) First, the patient must demonstrate chronic GI symptoms, i.e., symptoms that have lasted for seven days or more, because that duration suggests the symptoms are consistent with gastroparesis and inconsistent with illnesses of shorter duration like gastroenteritis. (*Id.* at 40:8–12, 40:25–41:2.)

Second, the patient must not have symptoms or a history suggestive of other diagnoses associated with chronic GI symptoms. Dr. Raines explained that potential alternative diagnoses include psychological disorders (anorexia and bulimia), organic disorders (gastric cancer, gastric ulcer, gallstones, pancreatitis), disorders of the gut-brain interaction (functional dyspepsia, chronic nausea and vomiting syndrome, clinical vomiting syndrome, cannabinoid hyperemesis syndrome, and rumination syndrome), and other subsets of gastroparesis. (*See* May 14, 2025 Pt. 1 Tr. at 29:24–47:16.) When ruling out other potential diagnoses, a physician must consider whether there is evidence that the patient’s symptoms are caused by a mechanical obstruction, including symptoms suggestive of gastric cancer or gastric ulcer, or that the patient has history of gastric obstructions. (*Id.* at 101:24–104:10.) Absent any evidence suggestive of a mechanical obstruction, Dr. Raines opines that the physician can exclude that as a potential cause and find the second gastroparesis requirement satisfied. (*Id.*)

Third, there must be a temporal association between the onset of symptoms and the patient’s initiation or titration of a GLP-1 RA. (*Id.* at 129:19–24 (“Q. So you’re saying there is a temporal component to the symptoms that you need? A. Correct. In the case of drug-induced gastroparesis, I’m adding an additional criteria, which is that there has to be a relationship where

the symptoms either began or became much worse on the drug.”). Dr. Raines explained that the timing is important because a patient who had symptoms before beginning the medication is less likely to have gastroparesis because of the medication, as is a patient whose symptoms developed more than three months after they began using the GLP-1 RA. According to Dr. Raines, the timing also suggests that the medication’s effect on gastric emptying is likely causing the patient’s symptoms, such that the symptoms themselves are evidence of delayed emptying. (*Id.* at 250:8–12 (stating that he is “relying on documented evidence that GLP-1 RAs can delay gastric emptying”); Raines Dep. Tr. at 137:4–144:9 (testifying that “symptoms suffered in correlation with a GLP-1 RA” are evidence of delayed emptying).) Similarly, the presence of retained gastric food—either the vomiting of undigested food four hours after ingestion or the presence of undigested food on an imaging study such as a CT scan, ultrasound, or endoscopy—also serves as evidence of delayed emptying, and by extension, suggests the patient has drug-induced gastroparesis. (May 14, 2025 Pt. 1 Tr. at 56:23–57:5 (describing “routine vomiting of undigested food” or a “study . . . that demonstrates retaining food, like an imaging study or an endoscopy” as “objective findings of delayed gastric emptying”); *see also id.* at 13:11–18, 54:12–55:5, 70:13–74:3, 82:2–16, 125:10–16, 250:13–17; Raines Dep. Tr. at 107:13–17, 117:20–24, 120:16–23, 130:16–19, 186:11–20, 212:16–19.)

At the end of this process, if the three criteria are met, Dr. Raines finds the patient has “a typical presentation of drug-induced gastroparesis”<sup>13</sup> (i.e., “they’re vomiting undigested food,

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<sup>13</sup> During his deposition, Dr. Raines conceded that this portion of his methodology is somewhat “circular,” in that the “more classic the[ patient’s] presentation is for drug-induced gastroparesis” in terms of symptoms, the “more likely” he is to diagnose them with drug-induced gastroparesis. (Raines Dep. Tr. at 142:2–8 (“Q: It seems circular to me, sir. A: I know, me, too.”).) *See Soldo*, 244 F. Supp. 2d at 519 (“Dr. Kulig’s basis for ruling out idiopathic causes of plaintiff’s ICH—his belief that there was an obvious alternative explanation for the stroke in that plaintiff had taken Parlodel—is fatally circular.”).



they don't have any imaging study or anything else, and they don't have any signs or symptoms or risk factors for any other pathology") and reasons that the physician can diagnose the patient with drug-induced gastroparesis and should treat the patient by withdrawing their GLP-1 RA. (May 14, 2025 Pt. 1 Tr. at 127:14–20.) If the patient later returns and is continuing to experience symptoms despite being off the medication, something Dr. Raines estimates happens around 10% of the time in his own practice,<sup>14</sup> then the physician should reevaluate the diagnosis and move forward with objective testing, including an endoscopy to confirm absence of medical obstruction and a gastric emptying study to confirm delayed gastric emptying. (*See id.* at 98:5–22 (testifying that if a patient previously diagnosed with drug-induced gastroparesis continues to experience symptoms three weeks after being taken off the drug, Dr. Raines “would go directly through th[e] algorithm. So I would do an upper endoscopy next and then I would do a GES” and conceding he would not perform a CAT scan, an MRI, an ultrasound, or an x-ray to confirm delayed emptying).)

## 2. Standard Diagnostic Techniques

Defendants argue that Dr. Raines's differential diagnosis is nothing more than a symptoms-based methodology that is contrary to clinical guidelines. (Doc. No. 360-1 at 18, 21; Doc. No. 361-1 at 23–25.) According to Defendants, the medical consensus shows that a patient *cannot* be diagnosed with any subset of gastroparesis—including drug-induced gastroparesis—without an endoscopy or other imaging study to rule out mechanical blockage *and* one of the three approved gastric emptying tests to confirm delayed emptying. (*See* Doc. No. 361-1 at 9–12, 18–25.) Plaintiffs counter that Dr. Raines's methodology is consistent with the medical

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<sup>14</sup> During the evidentiary hearing, Dr. Raines admitted he has not counted his patients, nor does he have data to confirm this estimate. (*See* May 14, 2025 Pt. 1 Tr. at 144:25–146:8.)

consensus because the relevant guidelines focus on other subsets of gastroparesis, not drug-induced gastroparesis, and to the extent any guideline does apply in the drug-induced context, Dr. Raines’s methodology comports with recommendations that any patient on a GLP-1 RA be taken off the medication before a gastric emptying study is performed. (Doc. No. 379 at 6–7, 10, 16, 22.)

The parties have conducted a comprehensive literature review and submitted more than 50 articles from medical journals that discuss the diagnosis and treatment of gastroparesis, including multiple guidelines published by domestic and international organizations that specialize in gastroenterology. Those guidelines consistently state that *objective testing* to exclude mechanical obstruction and to confirm delayed emptying is *required* before a physician can diagnosis gastroparesis. *See, e.g., 2013 ACG Guideline* at 21 (“Documented delay in gastric emptying is *required* for the diagnosis of gastroparesis. . . . There are *three tests* to objectively demonstrate delayed gastric emptying: scintigraphy, wireless motility capsule (WMC), and breath testing.” (emphases added)); *2020 UEG & ESNM Consensus* at 287 (“The panel agreed that an upper endoscopy and a [gastric emptying] test are *required* for diagnosis.” (emphasis added)); *2025 Rome Consensus* at 70 (“By definition, gastroparesis implies an objective delay in gastric emptying in the absence of mechanical obstruction, and *requires* both an assessment of gastric emptying and confirmation of the absence of gastric outlet obstruction or another mechanical factor most commonly through an upper endoscopy.” (emphasis added)); *id.* at 76 (“When making a diagnosis of gastroparesis, a selected panel of laboratory tests, an abnormal gastric emptying test, and a normal upper endoscopy are *mandatory*.” (emphasis added)); *cf.* *2022 ACG Guideline* at 1197 (stating “mechanical obstruction . . . should be excluded by imaging studies such as upper gastrointestinal (GI) endoscopy or radiology”); *id.* at 1199

(recognizing scintigraphy as the “standard test for the evaluation of GP [gastroparesis] in patients,” but recommending WMC and breath test as reliable alternatives).<sup>15</sup>

As noted above, Dr. Raines disagrees that either an endoscopy or a gastric emptying test is required to diagnose drug-induced gastroparesis. (*See* May 14, 2025 Pt. 1 Tr. at 96:23–97:5 (“The Court: So you are willing to assign this diagnosis just based on what they come in and tell you; didn’t have any [symptoms] before [starting the drug]; you’ve taken their family history; you’ve taken their personal history. You’re willing to assign the drug-induced gastroparesis diagnosis right then without any objective testing? [Dr. Raines]: Yes, Your Honor.”).) When presented with the guidelines’ contrary conclusions, Dr. Raines attempted to limit their application, testifying that neither the *2022 ACG Guideline* nor the *2025 Rome Consensus* applies to *drug-induced* gastroparesis. (May 14, 2025 Pt. 1 Tr. at 141:6–13 (*2022 ACG Guideline*); *id.* at 165:10–22 (*2025 Rome Consensus*).) A review of the *2025 Rome Consensus* confirms that its focus was “idiopathic gastroparesis” (i.e., gastroparesis of unknown origin), but nowhere does it state its methods for diagnosis are inapplicable to other subsets of gastroparesis. *See 2025 Rome Consensus* 68 (providing a “consensus on the definition and management of idiopathic gastroparesis”). Similarly, although the *2022 ACG Guideline* states that the authors were not focused on the association between gastroparesis and “use of narcotics in pain syndromes” or the effect of opioid agents on gastric emptying, the authors broadly define their

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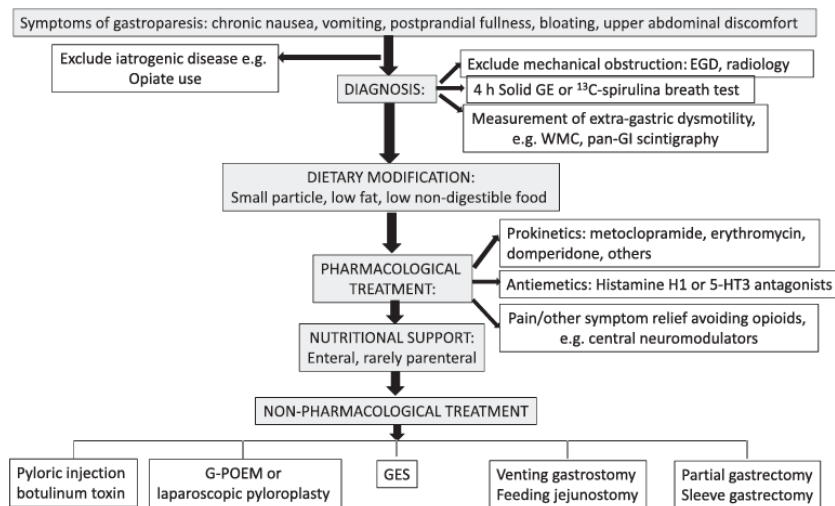
<sup>15</sup> This case thus involves a different medical landscape than the one the Third Circuit encountered in *Paoli*. In that case, the court’s reliability analysis was influenced by its recognition that “although differential diagnosis is a generally accepted technique” for determining the cause of a patient’s illness, “the medical community will rarely have considered the reliability of a particular process of differential diagnosis used in an individual case. Nor is it likely that the particular combination will have been published and subject to peer review, because a particular version of differential diagnosis will rarely be of general interest to the medical community.” *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d at 758; *see also Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 155 (3d Cir. 1999) (recognizing that physicians may reach a reliable diagnosis “even in those cases in which peer-reviewed studies do not exist to confirm the diagnosis of the physician”).

objective as “document[ing], summariz[ing], and updat[ing] the evidence and develop[ing] recommendations for the clinical management of GP [gastroparesis]” generally, without limiting the guideline to one specific subset. *2022 ACG Guideline* at 2–3.

Even if the Court agreed with Dr. Raines that these two guidelines are irrelevant in the drug-induced context and excluded them from consideration, Dr. Raines has not explained why the Court should disregard the recommendations of the other guidelines, which state an upper endoscopy or other imaging study to exclude mechanical obstruction and a gastric emptying test to confirm delayed emptying are *required* for diagnosis. *See, e.g., 2020 UEG & ESNM Consensus* at 287 (“The panel agreed that an upper endoscopy and a [gastric emptying] test are *required* for diagnosis.” (emphasis added)); *2013 ACG Guideline* at 21 (“Documented delay in gastric emptying is *required* for the diagnosis of gastroparesis. . . . There are *three tests* to objectively demonstrate delayed gastric emptying: scintigraphy, wireless motility capsule (WMC), and breath testing.” (emphases added)). Although Dr. Raines argues that none of the guidelines are meant to be “comprehensive,” and instead, describe only a “typical presentation” (May 14, 2025 Pt. 1 Tr. at 64:4–20), he has not explained why drug-induced gastroparesis falls outside of that “typical” presentation or should be evaluated differently. And at least one guideline, the *2020 UEG & ESNM Consensus*, recognizes drug-induced gastroparesis as one of many subsets of gastroparesis, but does not exclude or differentiate that subset from its broader conclusion that an endoscopy and a gastric emptying study are required to diagnose gastroparesis. *See 2020 UEG & ESNM Consensus* at 301.

In the alternative, Dr. Raines attests that even if the guidelines govern drug-induced gastroparesis, his proposed methodology is consistent with their recommendation that patients be taken off medications that are known to affect gastric emptying, like GLP-1 RAs, before a

physician conducts a gastric emptying study. (See Raines Dep. Tr. at 174:10–15 (“Q: When they write: ‘Exclude iatrogenic disease,’ they mean stop opioids or GLP-1 RAs? A: Yeah. Q: And that’s what you infer to mean that you can diagnose gastroparesis based on history and physical alone? A: I think it’s supportive of that conclusion.”); see also May 14, 2025 Pt. 1 Tr. at 80:16–25, 223:7–12).) See, e.g., 2022 ACG Guideline at 1200–01 (“It is customary to recommend cessation for 48 hours before the test of medications including opioids, cannabinoids, prokinetics, antiemetics, and neuromodulators with potential impact on the results of the GE test.”); 2012 ACG Guideline at 21 (“For any type of gastric emptying test, patients should discontinue medications that may affect gastric emptying. . . . These include medications that can delay gastric emptying,” which “may give a falsely delayed result. Medications that accelerate gastric emptying . . . may give a falsely normal result.”). For example, many of the guidelines reflect that recommendation in algorithms like the following:



**Figure 1.** This algorithm updates the algorithm from the 2013 ACG guideline on gastroparesis (1). ACG, American College of Gastroenterology, EGD, esophagogastroduodenoscopy; GE, gastric emptying; GI, gastrointestinal; G-POEM, gastric per-oral endoscopic myotomy; WMC, wireless motility capsule.

2022 ACG Guideline at 1198.

But, as Dr. Raines concedes, this recommendation goes to management, not diagnosis, of a patient displaying symptoms consistent with gastroparesis. (May 14, 2025 Pt. 1 Tr. at 82:22–

25 (recognizing the guidelines’ algorithms reflect a “recommended way of management”); *see also* Raines Dep. Tr. at 204:2–24 (conceding that the guidelines’ direction to discontinue drugs that interfere with gastric emptying is not the same as a direction to diagnose the patient with drug-induced gastroparesis).) In other words, if a patient presents with upper GI symptoms while on a medication that is known to cause such symptoms, the first step in management is to take the patient off the potentially offending drug. (May 14, 2025 Pt. 1 Tr. at 65:9–21.) As Dr. Raines explains, it would make little sense (and be “inappropriate”) to keep the patient on a medication that seems to be making them ill while they wait weeks for the physician to order the radioactive tracer used in a scintigraphy study, because even if that test confirms the physician’s suspicion that the patient has drug-induced gastroparesis, the treatment plan would be the same: withdraw the medication. (*Id.*) By withdrawing the medication as the first step, some patients find their symptoms resolve without suffering the wait and potential expense associated with a gastric emptying study. And even if the patient’s symptoms remain after the medication is withdrawn, it advances the ultimate treatment goal of symptom resolution because the physician can then perform the gastric emptying study without potential confounding by a medication that is known to alter gastric emptying rates but does not appear to be the cause of the patient’s symptoms. (*See id.* at 65:9–66:22, 98:5–22; *see also* May 14, 2025 Pt. 2 Tr. at 114:13–24 (Dr. Nguyen discussing similar method of treatment).)

The problem, though, is that even if Dr. Raines’s methodology is consistent with the standard process for *treating* patients suspected of suffering from drug-induced gastroparesis, it is at odds with the medical consensus on what inputs are required to reliably *diagnose* a patient with gastroparesis, including the drug-induced gastroparesis subset. Courts have recognized that treatment and diagnosis may be distinct issues. *See Hoeftling v. U.S. Smokeless Tobacco Co.*,

576 F. Supp. 3d 262, 282 (E.D. Pa. 2021) (“To the extent Hoefling’s experts defend the decision not to attempt another biopsy, they do so on pragmatic grounds: Hoefling’s physician may have foregone further testing because Hoefling’s *treatment* would have been the same regardless of his cancer’s cause. That may be true, but it does not diminish the importance of a biopsy for determining the *cause* of his cancer.” (internal citations omitted)); *cf. Soldo*, 244 F. Supp. 2d at 528–29 (“Without sufficient reliable evidence of general causation, plaintiff’s experts could not reliably apply a differential diagnosis that comports with the scientific method, notwithstanding the fact that physicians in clinical practice may be required to proceed with a differential diagnosis on the basis of guesses or hypotheses due to the exigency of the need to treat their patients.”).

That does not necessarily mean that Dr. Raines’s proposed differential diagnosis is unreliable. Instead, it means that Dr. Raines must offer a “good explanation as to why” any conclusion reached using his methodology “remain[s] reliable” despite its departure from standard techniques. *In re Paoli*, 35 F.3d at 760; *see also id.* at 761 (“[T]he opinion of a doctor who has engaged in few standard diagnostic techniques should be excluded unless the doctor offers a good justification for his or her conclusion.”). It is to this question that the Court turns next.

### 3. Good Grounds

Dr. Raines testified that his proposed method for diagnosing drug-induced gastroparesis is reliable, despite its departure from standard diagnostic techniques, because through a thorough physical examination and patient history, a physician can find all three gastroparesis requirements satisfied and exclude other potential diagnoses to reach a conclusion that drug-induced gastroparesis is the most likely diagnosis. (*See* May 14, 2025 Pt. 1 Tr. at 21:22–47:16.)

Defendants disagree and argue that Dr. Raines has not met his burden of showing the reliability of his proposed methodology. (Doc. No. 360-1 at 20–26; Doc. No. 361-1 at 19–25.)

“The requirement of reliability, or ‘good grounds,’ extends to each step in an expert’s analysis, all the way through the step that connects the work of the expert to the particular case.” *In re Paoli*, 35 F.3d at 743; *see also Heller*, 167 F.3d at 155 (“We have held that the reliability analysis applies to all aspects of an expert’s testimony: the methodology, the facts underlying the expert’s opinion, the link between the facts and the conclusion, *et alia*.”). That means that “to avoid exclusion of his . . . opinion,” Dr. Raines must show that the criteria underlying his differential diagnosis provide “good grounds” for a physician to diagnose a patient with drug-induced gastroparesis. *In re Paoli*, 35 F.3d at 761. Here, Defendants argue that Dr. Raines’s methodology is not based on “good grounds,” because it rests on two unreliable assumptions about how to reliably find a patient is suffering from delayed gastric emptying: (1) the presence of retained gastric food is objective evidence of delayed gastric emptying; and (2) a temporal connection between symptoms and GLP-1 RA initiation or titration is objective evidence of delayed gastric emptying. (See Doc. No. 360-1 at 24–26; Doc. No. 361-1 at 19–23.)<sup>16</sup> They also argue that Dr. Raines’s methodology is unreliable because it does not account for the alternative diagnosis of functional dyspepsia. (Doc. No. 360-1 at 8–9; Doc. No. 361-1 at 9–10,

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<sup>16</sup> As noted above, during the May 14, 2025 hearing, Defendants challenged Dr. Raines’s opinion that he can reliably diagnose drug-induced gastroparesis without conducting an endoscopy or other imaging study to confirm a lack of mechanical obstruction. Dr. Raines testified that he confirms the absence of a mechanical obstruction by conducting a physical and taking a patient history that considers whether the patient has symptoms consistent with a mechanical obstruction and listening to the patient’s abdomen for a succussion splash. Although the Court has found these methods to be contrary to standard diagnostic techniques used by physicians to diagnose a patient with gastroparesis, the parties have provided little argument about whether these techniques may nevertheless provide “good grounds” for a physician to reliably confirm the absence of a mechanical obstruction. And because the Court finds Dr. Raines’s proposed methodology is unreliable for other reasons, the Court does not discuss his opinions about mechanical obstruction in this section.



19, 25.) The Court addresses the reliability of Dr. Raines’s assumptions about delayed gastric emptying before turning to whether his method reliably accounts for alternative diagnoses.

*a. Assumptions Surrounding Delayed Gastric Emptying*

First, Defendants argue that Dr. Raines’ methodology is not based on “good grounds” because it rests on the unreliable assumption that a physician can find a patient is suffering from delayed gastric emptying based purely on (1) the presence of retained gastric food, or (2) symptoms and timing.

*i. Evidence of Retained Gastric Food*

Dr. Raines opines that evidence of retained gastric food can serve as evidence of delayed emptying. (May 14, 2025 Pt. 1 Tr. at 13:11–18, 54:12–55:5, 56:23–57:5, 70:13–74:3, 82:2–16, 125:10–16, 250:13–17; Raines Dep. Tr. at 107:13–17, 117:20–24, 120:16–23, 130:16–19, 186:11–20, 212:16–19.) According to Dr. Raines, the presence of undigested food in the stomach more than four hours<sup>17</sup> after the patient has finished a meal is evidence of delayed gastric emptying. (May 14, 2025 Pt. 1 Tr. at 78:8–11, 126:12–21.) Dr. Raines identified multiple tests that physicians can use to “look[ ] for retained food in the stomach,” including “ultrasound, MRI, CT, x-ray,” and “upper endoscopy.” (*Id.* at 54:12–55:5; *see also id.* at 78:8–11 (“And when we observe evidence of retained gastric food on endoscopy or imaging, CAT scan, ultrasound, then we consider that evidence of delay.”).) He clarified, however, that a physician does not need to perform any such tests and can find a patient has abnormal retained

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<sup>17</sup> There was some inconsistency with Dr. Raines’s testimony on timing. On direct examination during the evidentiary hearing, Dr. Raines was adamant that all solid foods are expected to be digested within four hours (May 14, 2025 Pt. 1 Tr. at 10:1–11:6), but on cross-examination, he conceded that many factors could affect how long it takes for food to digest (*id.* at 218:9–222:18 (noting that alcohol, medications, and “laying in bed,” among “other things,” can cause delayed emptying, such that undigested food would remain after four hours)).

gastric food—and therefore, delayed gastric emptying—solely from the fact that the patient is vomiting undigested food hours after finishing a meal. (*Id.* at 82:2–16, 125:17–126:21.)

Dr. Raines argues that he has good grounds for the assumption that retained gastric food is evidence of delayed emptying because it is supported by two peer-reviewed retrospective studies. (*See id.* at 75:4–77:19. *But see* Raines Dep. Tr. at 221:1–4 (testifying that he was unable to identify any studies that show the presence of retained gastric food is a reliable predictor of delayed gastric emptying).) But Dr. Raines takes the conclusions of these studies further than the authors themselves were willing to go.

A review of each study is helpful. In the first, which we will refer to as “*Coleski 2016*,” the authors conducted a retrospective investigation to determine whether the literature suggested a correlation between “the prevalence and degree of food retention on upper endoscopy with underlying diseases, gastric emptying rates, and medication use patterns.” Radoslav Coleski et al., *Endoscopic Gastric Food Retention in Relation to Scintigraphic Gastric Emptying Delays and Clinical Factors*, 61 Digestive Diseases and Sciences 2593, 2594 (2016). As relevant here, the authors considered the records of 103 patients who had retained gastric food on endoscopy, and who had also undergone gastric scintigraphy. *Id.* at 2595. Seventy-six of the 103 patients (74%) “exhibited gastric emptying delays.” *Id.* The authors concluded that this “study show[ed] a close association of retained gastric food residue to delays in gastric emptying.” *Id.* at 2598. And in particular, the data “suggest[ed] that gastric scintigraphy may not be needed to document emptying impairments in patients with non-obstructive causes of gastric food retention on endoscopy.” *Id.* at 2599.<sup>18</sup> The authors did not, however, go so far as to say

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<sup>18</sup> The authors also considered a second cohort of 619 patients who had delayed gastric emptying. *Coleski 2016* at 2595. They found that 164 of the 619 patients (26%) in that cohort had evidence of retained gastric food on endoscopy. *Id.* According to the authors, these “findings suggest that most patients with gastroparesis are ultimately able to clear their stomach of meal residue.” *Id.* at

physicians could reliably look to retained gastric food as a substitute for scintigraphy, asserting instead that the “issue warrants consideration by a panel of experts in future consensus documents on management of gastric emptying delays.” *Id.*; *see also id.* at 2600 (describing their observations as “hav[ing] clinical relevance” and “form[ing] a foundation for further investigation”).

Four years later, a second study was published, which we will refer to as “*Bi 2020*.” *See* Danse Bi et al., *Food Residue During Esophagogastroduodenoscopy Is Commonly Encountered and Is Not Pathognomonic of Delayed Gastric Emptying*, 66 *Digestive Diseases and Sciences* 3951, 3951–59 (2021) (published online November 2020). *Bi 2020* discussed the findings of *Coleski 2016* and noted that in the previous study, only 43 patients had data regarding gastric emptying at four hours. *Id.* at 3952.<sup>19</sup> “Given that the prevalence, etiology, and significance” of retained gastric food on endoscopy “remain[ed] unclear” following *Coleski 2016*, the *Bi 2020* retrospective aimed: “[1] to identify the prevalence of [retained gastric food] in patients undergoing [endoscopy], [2] to determine whether [retained gastric food] is associated with delayed [gastric emptying], and [3] to evaluate the relationship between [retained gastric food] and medications associated with delayed [gastric emptying].” *Id.*

The authors reviewed 2,991 electronic medical records for adult patients who underwent an endoscopy and a scintigraphy study between October 2012 and September 2018. *Id.* at 3953. They found that in “the entire cohort,” i.e., all 2,991 patients, the positive predictive value (“PPV”) of “retained gastric food for delayed gastric emptying was 55%.” *Id.* Where the cohort

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2599; *see also id.* (finding that the data was “consistent with the interpretation that the absence of endoscopic food retention is not equivalent to normal gastric emptying”).

<sup>19</sup> *Coleski 2016* itself recognized one limitation of its retrospective investigation was the use of “non-standardized scintigraphic methods recorded on some patients.” Coleski, et al., *Coleski 2016* at 2600.

was categorized by prior medical condition, however, that percentage shifted, such that in patients with type 1 diabetes, the PPV of retained gastric food for delayed gastric emptying was 79%; in patients with type 2 diabetes, the PPV was 67%; in patients with a preexisting diagnosis of gastroparesis, the PPV was 71%; in patients with amyloidosis, the PPV was 100%; and where the patient had none of these preexisting conditions, the PPV was only 32%:

**Table 3** The relationship between medical conditions, RGF, and delayed GE in patients who had undergone EGD and GES

	N (%)	%RGF	%GE2	%GE4	%DGE	PPV of RGF for DGE (%)	NPV of RGF for DGE (%)
All patients	2991 (100%)	7	45 ± 21%	80 ± 23%	30	55	72
Type 1 diabetes mellitus	125 (4%)	22***	40 ± 24%*	70 ± 30%***	45***	79	65
Type 2 diabetes mellitus	142 (5%)	13**	47 ± 25%	76 ± 26%	36	67	69
Gastroparesis	687 (22%)	14***	33 ± 19%**	67 ± 24%***	61***	71	41
Amyloidosis	47 (2%)	9	40 ± 17%	79 ± 21%	36	100	70
No risk factors for delayed GE	2150 (72%)	4	48 ± 20%	83 ± 21%	20	32	80

%GE2 % gastric emptying at 2 h, %GE4 % gastric emptying at 4 h, %DGE % of patients with delayed gastric emptying, *DGE* delayed gastric emptying, *OR* odds ratio, *PPV* positive predictive value, *NPV* negative predictive value. \* $P \leq 0.05$  relative to the absence of the condition, \*\* $P \leq 0.01$  relative to the absence of the condition, \*\*\* $P \leq 0.001$  relative to the absence of the condition

*Id.* at 3954, Tbl. 3; *see also id.* at 3956. The authors concluded that “[t]aken together, these findings suggest that [retained gastric food] can only be used as a surrogate for delayed [gastric emptying] or a diagnosis of gastroparesis in select patient cohorts with a high pretest probability (e.g., patients with type 1 diabetes).” *Id.* at 3958. For the remaining cohorts “[f]urther evaluation with a formal, validated [scintigraphy study] . . . is *required* . . . as [retained gastric food] is *not* pathognomonic of delayed [gastric emptying].” *Id.* (emphases added); *id.* at 3957, Fig. 2 (algorithm which allows physicians to find retained gastric food suggestive of “probable delayed [gastric emptying]” without further investigation only in patients with type 1 diabetes).

As this overview suggests, Dr. Raines takes the conclusions of *Coleski 2016* and *Bi 2020* too far when he cites them as supporting his conclusion that retained gastric food is pathognomonic of delayed gastric emptying. In other words, “there is simply too great an analytical gap” between the research cited “and the opinion proffered.” *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997); *id.* at 145 (“Given that Bertazzi et al. were unwilling to say

that PCB exposure had caused cancer among the workers they examined, their study did not support the experts' conclusion that Joiner's exposure to PCB's caused his cancer."); *id.* at 146–47 (holding that “because it was within the District Court’s discretion to conclude that the studies upon which the experts relied were not sufficient, whether individually or in combination, to support their conclusions that Joiner’s exposure to PCB’s contributed to his cancer, the District Court did not abuse its discretion in excluding their testimony”).

Consistent with the conservative conclusions of both *Coleski 2016* and *Bi 2020*, guidelines since 2020 have maintained that retained gastric food is *not* diagnostic of delayed gastric emptying or gastroparesis. *See 2025 Rome Consensus* at 70 (“Clinically, food retention in the stomach on endoscopy after an overnight fast has been used as a probable sign of gastroparesis. However, the one study correlating this retention with gastric emptying testing showed it lacks accuracy.” (citing *Coleski 2016*)); *2022 ACG Guideline* at 1202 (“Retained gastric food (RGF) is frequently identified during esophagogastro-duodenoscopy; however, this should not be deemed to be diagnostic of [gastroparesis].” (referencing *Bi 2020*)); *2020 UEG & ESNM Consensus* at 293 (declining to endorse the statement that the “presence of food in fasting state during endoscopy is diagnostic for gastroparesis” (citing *Coleski 2016*)).

Outside of these guidelines, experts in the field have similarly read *Coleski 2016* and *Bi 2020* as standing for the proposition that retained gastric food cannot be considered diagnostic of delayed gastric emptying or gastroparesis. *See* David J. Cangemi et al., *Misdiagnosis of Gastroparesis is Common: A Retrospective Review of Patients Referred to a Tertiary Gastroenterology Practice*, 21 *Clinical Gastroenterology and Hepatology* 2670, 2671 (2023) (filed as Doc. No. 360-11) (“*Misdiagnosis*”) (“Although findings of retained gastric food on upper endoscopy were seen more commonly in patients correctly diagnosed with [gastroparesis]

in our study, it is important to highlight that the presence of retained food on EGD is not diagnostic of [gastroparesis].” (citing *Bi 2020*)); Michael Camilleri et al., *A N. Am. Perspective on the ENSM Consensus Statement on Gastroparesis*, 33 *Neurogastroenterology and Motility* 1, 4 (2021) (filed as Doc. No. 360-14) (“*N. Am. Perspective*”) (“We agree with the endorsements by the ESNM working group,” in the *2020 UEG & ESNM Consensus*, “regarding the diagnosis of gastroparesis, specifically, exclusion of gastric or small intestinal obstruction, upper gastrointestinal endoscopy, and gastric emptying testing (by scintigraphy or breath test, but not by wireless motility capsule), being mandatory for establishing a diagnosis of gastroparesis, although *the presence of food in the fasting state during endoscopy is not sufficient for diagnosis.*” (emphasis added)); Dept. of Health & Human Servs. et al., *Pharmacovigilance, Epidemiology, and Drug Utilization Review* at 2 (Dec. 14, 2023) (filed as Doc. No. 360-16) (“*HHS Review*”) (“Additional methods of evaluation (e.g., upper gastrointestinal [GI] endoscopy, computed tomographic enterography, magnetic resonance enterography, or barium follow-through examination) can assist in determining the presence of mechanical obstruction or food retention after an overnight fast; however, these evaluations do not assess gastric motility and the presence of retained food is considered supportive but not diagnostic for [gastroparesis].” (citing *Bi 2020*)).

Plaintiffs argue that Dr. Raines’s assumption about retained gastric food is nevertheless reliable because it is supported by two recently published case reports, which show physicians rely on this assumption in practice when diagnosing patients taking GLP-1 RAs with drug-induced gastroparesis. (Doc. No. 379 at 30 n.121.) But those case reports are merely summaries of a specific patient’s presentation and treatment by a particular physician. They are not research studies or broadly accepted guidance documents outlining an accepted method of

diagnosis. *See Soldo*, 244 F. Supp. 2d at 484 (“Dr. Kulig’s methodology reasons from anecdotal data, the error rate of which is impossible to know or establish. He admits that case reports are not controlled, blinded, capable of yielding statistical significance, or capable of ruling out other alternative causes of the events noted therein.”). Nor have Plaintiffs shown that the case reports are the type of documents on which physicians or experts rely.<sup>20</sup> And even if they were, they do not support Dr. Raines’s conclusion that retained gastric food is a reliable indicator of delayed emptying. Notably, in both cases, the physicians acknowledged that “[p]roof of delayed gastric emptying in gastric emptying studies is required for diagnosis” and they spoke of their diagnoses as merely “possible” or “suspected” in the absence of such a study. Ahtshamullah Chaudhry et al., *Tendency of Semaglutide to Induce Gastroparesis: A Case Report*, Cureus (Jan. 19, 2024) (filed as Doc. No. 379-17) (concluding that there is a “need to recognize medication-induced gastroparesis as a *possible* diagnosis” when a patient experiences GI symptoms that improve once the use of a GLP-1 RA is discontinued (emphasis added)); Puja Rai et al., *Liraglutide-induced Acute Gastroparesis*, Cureus (Dec. 28, 2018) (“In *suspected* gastroparesis, an upper endoscopy is indicated to exclude a mechanical obstruction. In addition, a four-hour, solid-phase gastric emptying scintigraphy test to assess gastric retention is recommended to confirm the diagnosis. . . . Drug-induced gastroparesis, specifically with liraglutide use, should be *considered* in patients presenting with significant abdominal distension, pain, and nausea

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<sup>20</sup> Tellingly, Plaintiffs’ other expert, Dr. Siegel, testified during the evidentiary hearing that “in no way would the fact that somebody has a case report sway me from the well-established guidelines for the society and all of the community standard accepted practice.” (May 14, 2025 Pt. 2 Tr. at 88:16–23; *see also id.* at 89:4–14 (“I mean, the fact that somebody was willing to do it and then wrote up the results of it, I mean, more power to them for essentially sharing what they did and what they found. But in no way would the fact that somebody was willing to” perform a scintigraphy test on a patient taking GLP-1 RAs “sway my opinions. The fact that one publishes a case report would have minimal impact on my opinions whether it’s someone who does peer review or someone who edits a journal.”).)

once mechanical obstruction has been ruled out. It should be *suspected* in diabetic patients with recent liraglutide initiation . . . .” (emphases added)). There may be a situation where case studies could show that there are good grounds for an expert’s opinion, but we cannot find so here, especially not in the face of the published studies and guidance documents discussed above.

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In sum, Dr. Raines’s assumption that retained gastric food is pathognomonic of delayed gastric emptying is not generally accepted in the medical community, and to the extent the hypothesis has been tested, the results of that testing suggest that the PPV of retained gastric food is 67% at best and 32% at worst for the cohorts relevant to Plaintiffs in this MDL. The references on which Dr. Raines relies do not support his ultimate assumption, and he has not otherwise shown that his assumption is reliable. Accordingly, Dr. Raines’s proposed differential diagnosis is excluded as unreliable to the extent it rests on this assumption.

ii. Symptoms Within Three Months of Drug Initiation or Titration

Dr. Raines also opines that a physician can reliably find a patient suffers from delayed gastric emptying if the patient develops GI symptoms within three months<sup>21</sup> of starting or

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<sup>21</sup> The exact timing shifted during Dr. Raines’s testimony at his deposition and during the evidentiary hearing, ranging from one week, to one month, to five weeks, before eventually settling on an outer limit of three months. (See Raines Dep. Tr. at 207:14–22 (one week); May 14, 2025 Pt. 1 Tr. at 129:25–130:6 (“I don’t have a number for that . . . the typical is a few weeks later . . . . I don’t have research to demonstrate it occurs at this time or this time. But the typical patient it is about a month later.”); see also *id.* at 130:17–21 (“three, four, five weeks”); *id.* at 131:6–11 (“within three months”); *id.* at 132:20–24 (“So if they didn’t have onset of symptoms or worsening of symptoms within three months of starting or within three months of changing—increasing the dose, then I would not follow the same—like I don’t need to do other testing.”)). To put it bluntly, Dr. Raines appeared to be reaching his opinion on the fly, as opposed to testifying about a settled and reliable temporal association. Although somewhat concerned by this testimony, the Court will nevertheless consider Dr. Raines’s ultimate assumption of three months for purposes of this Memorandum. Notably, three months is supported by peer-reviewed literature demonstrating that most patients taking a GLP-1 RA medication experience delayed gastric emptying, if at all, between five weeks and three months after they start taking the drug or increase their



titrating a GLP-1 RA medication. (Doc. No. 360-1 at 20–26; Doc. No. 361-1 at 19–23.) As a reminder, Dr. Raines broadly requires evidence of a close temporal proximity before he can find that a patient’s GI symptoms are “drug-induced.” (May 14, 2025 Pt. 1 Tr. at 129:19–24 (“Q. So you’re saying there is a temporal component to the symptoms that you need? A. Correct. In the case of drug-induced gastroparesis, I’m adding an additional criteria, which is that there has to be a relationship where the symptoms either began or became much worse on the drug.”).) But Dr. Raines’s methodology also rests, in part, on the assumption that a physician can reliably find a patient suffers from delayed gastric emptying based on that same temporal association. (See Raines Dep. Tr. at 137:4–141:18, 182:13–16; *accord* May 14, 2025 Pt. 1 Tr. at 132:20–24.) It is this latter assumption that Defendants challenge.

Dr. Raines asserts that his assumption is reliable because it is consistent with medical literature and the FDA-approved labels for certain GLP-1 RA medications, all of which recognize that this class of medications delays gastric emptying. In other words, Dr. Raines reasons that because GLP-1 RAs delay emptying, a physician can reliably conclude that any symptoms that begin within three months of drug initiation or titration are likely being caused by that mechanism of action. For two reasons, the Court finds this assumption unreliable.

*First*, although Dr. Raines’s assumption is a testable hypothesis—i.e., whether symptoms plus timing is a reliable indication that the patient is suffering delayed gastric emptying—he has not himself tested how often his assumption is correct. He cannot state the known or potential error rate of his assumption. (May 14, 2025 Pt. 1 Tr. at 227:21–24, 228:22–230:15, 231:15–232:18.) Indeed, on cross-examination during the evidentiary hearing, he was unable to identify

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dosage. (See *id.* at 133:24–134:20); see also Michael Camilleri et al., *Prevalence and Variations in Gastric Emptying Delay in Response to GLP-1 Receptor Agonist Liraglutide*, 32 *Obesity* 232, 232–33 (2023).

any peer-reviewed literature that has tested his hypothesis. (*Id.* at 230:16–231:5 (“Q: Okay. Now, when you formed your opinions in this case, Dr. Raines, you did not know what percentage of patients who experienced nausea and vomiting while taking a GLP-1 RA actually have delayed gastric emptying; isn’t that true? A: Yeah. I think the research is pretty sparse in that area, as far as symptoms and a GES.”); *accord* Raines Dep. Tr. at 212:24–214:5.)

On redirect examination, Dr. Raines identified one study, in which the authors performed a meta-analysis of the literature published between 2007 and 2017 that evaluated the association between gastric emptying and nausea, vomiting, early satiety/postprandial fullness, abdominal pain, and bloating. *See* Priya Vijayvargiya et al., *Association Between Delayed Gastric Emptying and Upper Gastrointestinal Symptoms: A Systematic Review and Meta-Analysis*, 68 Gut 804, 804–13 (2019) (filed as Doc. No. 379-13) (“*Vijayvargiya 2019*”). The authors of *Vijayvargiya 2019* recognized that the prior literature showed the “association of gastric emptying” with upper GI symptoms was “controversial,” with studies often reaching mixed results. *Id.* at 805 (referencing “numerous positive or negative studies”). On review, the authors concluded that these mixed results were due to a “significant difference between optimal and suboptimal gastric emptying test methods when comparing delayed gastric emptying with nausea and vomiting.” *Id.* at 804. When focusing only on those studies “using optimal gastric emptying test methodology,”<sup>22</sup> the authors found “there were significant associations between gastric emptying” and nausea, vomiting, abdominal pain, and early satiety/fullness in patients with upper GI symptoms generally, and between delayed gastric emptying and nausea and

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<sup>22</sup> “An optimal gastric emptying test method was defined as breath test or scintigraphy appraising the emptying of a solid meal, monitored for at least 3 hours, well-documented end points of interest, validated calculations, realistic results and absence of confounders in the interpretation of the results or association.” *Vijayvargiya 2019* at 805.

vomiting in patients with gastroparesis.<sup>23</sup> *Id.* at 807; *see also id.* at 810 (“This meta-analysis demonstrated the importance of using optimal gastric emptying test methods in seeking the association between gastric emptying and symptoms.”).

Although at first blush this conclusion seems to support Dr. Raines’s assumption about symptoms and timing as reliable indicators of delayed emptying, a review of the authors’ test parameters and discussion suggests the study offers only limited support for his conclusion that GI symptoms *associated with starting or titrating a GLP-1 RA* are necessarily caused by delayed emptying. Tellingly, the authors of *Vijayvargiya 2019* state that when they were selecting studies for review as part of the meta-analysis, they excluded any studies where the patient was using “medications that potentially alter both [upper GI symptoms] and gastric emptying such as narcotics.” *Id.* at 805; *see also id.* at 807 (excluding one study from the gastroparesis cohort because it contained a “medication confounder”). As the authors explain:

[A] number of studies were removed from the final analysis *because of concern that medication use may have altered both gastric emptying and the ability to assess [upper GI symptoms]*. For example, two scintigraphy studies from the same research group included 425 and 262 participants. After subdividing [upper GI symptoms] based on severity, the authors reported there were no significant differences in symptoms between those with normal and delayed gastric emptying. A careful appraisal of this study shows that ~45% of patients in the gastroparesis group had >30% gastric retention at 4 hours of a 2% fat, 200 kcal egg-substitute meal. Such retardation of gastric emptying is typical of patients with the most severe gastroparesis, or secondary to a drug effect. Indeed, medication use in the gastroparesis group in the study included 16% on anxiolytics, 39.2% antidepressants (15.1% tricyclic antidepressants) and 42.3% narcotics. These medications could certainly alter gastric emptying, and can influence the perception of [upper GI symptoms]. *These dual effects of medications in such a sizeable proportion of the gastroparesis cohort could conceivably*

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<sup>23</sup> The gastroparesis cohort included patients previously diagnosed with idiopathic, diabetic, and post-surgical gastroparesis (i.e., subsets of permanent or persistent gastroparesis). *Vijayvargiya 2019* at 805.

*confound the ability to assess the relationship between gastric emptying and [upper GI symptoms].*

*Id.* at 811 (emphases added). Moreover, in the studies that the authors did consider, they found that for “patients with documented gastroparesis”—the cohort most relevant for Dr. Raines’s opinions—the association of delayed gastric emptying and symptoms is “less clear” than in other cohorts. *Id.* at 808. They note that although there “may be an association with nausea and vomiting in this group of patients . . . , [d]ata with optimal gastric emptying test methodology [we]re limited,” such that this population “require[s] further evaluation before utility can be determined.” *Id.* at 808–09. Because the meta-analysis explicitly excluded any studies that considered patients on medications, like GLP-1 RAs, and found the association between delayed emptying and symptoms to be “less clear” in patients with gastroparesis, the study offers limited support for Dr. Raines’s assumption that *patients taking GLP-1 RAs* who experience severe upper GI symptoms have delayed emptying to the point that they can be reliably diagnosed with gastroparesis without objective testing.<sup>24</sup>

*Second*, and relatedly, there is a fatal flaw in Dr. Raines’s assumption that because delayed emptying is *a* logical conclusion, it is *the* most likely conclusion. *See Magistrini*, 180 F. Supp. 2d at 594 (noting that one factor relevant to the reliability analysis is “whether the expert has unjustifiably extrapolated from an accepted premise to an unfounded conclusion”); *see also Hoefling*, 576 F. Supp. 3d at 275 (“Dr. Busse makes ‘speculative leaps’ in claiming that a causal link exists simply because it is biologically plausible.”); *In re: Zostavax (Zoster Vaccine Live) Prods. Liab. Litig.*, 579 F. Supp. 3d 675, 679 (E.D. Pa. 2021) (“A medical expert,

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<sup>24</sup> And at most, this study supports a finding that there is an association between delayed emptying and *some* upper GI symptoms, i.e., nausea and/or vomiting, in patients with gastroparesis. *See Vijayvargiya 2019* at 804.

however, must do more than simply pronounce an opinion that Zostavax caused a plaintiff's injuries."). Importantly, Dr. Raines does not exclude other potential mechanisms of action whereby GLP-1 RAs cause upper GI symptoms. *See* Michael A. Nauck et al., *GLP-1 Receptor Agonists in the Treatment of Type 2 Diabetes — State of the Art*, 46 *Molecular Metabolism* 1, 1 (2020) (filed as Doc. No. 361-11) ("*State of the Art*") ("All GLP-1 RAs share common mechanisms of action: augmentation of hyperglycemia-induced insulin secretion, suppression of glucagon secretion at hyper- or euglycemia, deceleration of gastric emptying preventing large post-meal glycemic increments, and a reduction in calorie intake and body weight."); (*see also* May 14, 2025 Pt. 2 Tr. at 118:2–120:3 (Dr. Nguyen explaining how a medication's effects on the brain can cause nausea, vomiting, and abdominal pain). At the evidentiary hearing, Dr. Raines admitted he lacked any data to support his conclusion that GI symptoms were being caused by GLP-1 RAs' effects on delayed emptying as opposed to other mechanisms of action. (May 14, 2025 Pt. 1 Tr. at 176:9–14 ("Q. You don't have data to reach any reliable conclusion to a reasonable degree of medical certainty that symptoms you observed in a patient on a GLP-1 are actually occurring because of delayed gastric emptying, true? A. True."); *id.* at 209:18–23 ("Q. Before forming your opinion in this case, you did not do any research on whether GLP-1s are more likely to cause GI symptoms due to their effects on the brain versus their effects on delayed gastric emptying, did you? A. Not to form my opinion, no.").) This weighs against a finding of reliability. *See Magistrini*, 180 F. Supp. 2d at 603 (finding the expert's methodology "flawed" in part because "Dr. Ozonoff contends that all lymphohematopoietic cancers can be treated together for etiological purposes. Dr. Ozonoff simply does not provide sufficient scientific support for this theory. When pressed, he could not identify any literature that supported this proposition."); *In re Zostavax*, 579 F. Supp. 3d at 681 ("Dr. Poznansky has not

provided any grounds to rule out the reactivation of the wild-type virus as the cause of Mr. Bush's shingles, admittedly an obvious alternative cause advanced by Merck. Even if he properly ruled in Zostavax as the cause, Dr. Poznansky has at best reached second base without advancing to home plate. His opinion that Zostavax was the culprit without making any attempt to rule out the wild-type virus is simply an ipse dixit frowned upon by the Supreme Court.”).

Tellingly, the limited literature discussing the issue suggests the GI side effects of GLP-1 RAs may not be associated with delayed gastric emptying, but one of the medications' other mechanisms of action. *See State of the Art* at 11 (“Side effects most reported with GLP-1 RAs are nausea, vomiting, and diarrhea . . . . Since these symptoms can occur in fasting subjects, they are probably not related to the effects of GLP-1 RA treatment on gastrointestinal functions (e.g., deceleration of gastric emptying) but instead are caused by direct interactions with CNS GLP-1 receptors most likely located in the brain stem (area postrema).”); Daniel R. Quast, MD, et al., *Macronutrient Intake, Appetite, Food Preferences and Exocrine Pancreas Function After Treatment with Short- and Long-Acting Glucagon-Like Peptide-1 Receptor Agonists in Type 2 Diabetes*, 23 *Diabetes, Obesity and Metabolism* 2344, 2351 (2021) (“*Quast 2021*”) (“The retardation of gastric emptying during GLP-1 RA treatment is unrelated to gastrointestinal symptoms.”); cf. Ryan J. Jalleh et al., *Gastrointestinal Effects of GLP-1 Receptor Agonists: Mechanisms, Management, and Future Directions*, 9 *The Lancet Gastroenterology & Hepatology* 957, 961 (2024) (filed as Doc. No. 359-3 at Ex. L) (“*Jalleh 2024*”) (“The relationship between gastrointestinal symptoms and gastric emptying rate is weak, and therefore screening for the deleterious effects of [GLP-1 RAs] should involve measurement of gastric emptying of solids for a minimum of 3 or 4h.”). Just one year ago, the authors of *Jalleh 2024*

emphasized that more research is needed to determine whether upper GI symptoms in individuals taking GLP-1 RAs are caused by delayed gastric emptying:

GLP-1 RAs are known to often induce substantial upper gastrointestinal symptoms, which might compromise their use or necessitate slower dose escalation according to recommendations by regulatory agencies. Nevertheless, the mechanisms underlying these symptoms are only now being elucidated. Immunohistochemical studies have shown that GLP-1 receptors are present in appetite-regulating regions of the hypothalamus, the medulla oblongata, and the parietal cortex. The area postrema within the medulla mediates aversive sensations such as nausea, and stimulation of GLP-1 receptors in this region represents a possible mechanism. Although the majority of GLP-1 RAs do not cross the blood-brain barrier, they might interact with the central nervous system via the nodose ganglion, where the cell bodies for vagal afferents are located, and stimulation of GLP-1 receptors on intestinofugal neurons, which might result in inhibition of gastrointestinal motility. *Greater understanding of the effects of GLP-1 RAs on gastrointestinal and central nervous system function is clearly needed.*

*Jalleh 2024* at 960 (emphasis added).

When confronted with research stating that “GLP-1 RA effects, including their GI side effects, are caused primarily through mechanisms other than delayed gastric emptying,” Dr. Raines could not identify any data to support his contrary conclusion, and instead, continued to rely on evidence that a delay in gastric emptying is one mechanism of action for GLP-1 RAs. (May 14, 2025 Pt. 1 Tr. at 211:11–214:20; *see also id.* at 215:5–217:18 (discussing two other studies on which Dr. Raines relied for his opinion, both of which identify other mechanisms of action for GLP-1 RAs, including the drugs’ effects “on the vagus nerve and in the brain”).) And when asked how he could maintain that conclusion given the evidence that GI symptoms could be caused by the drugs’ effects on the brain, he acknowledged that GLP-1 RAs’ “central mediated effect would potentially describe or help explain nausea, but not any of the other symptoms associated with gastroparesis,” because “medications can make you nauseous, but”

they “don’t give people abdominal distension or bloating o[r] pain.” (*Id.* at 21:3–16; *see also id.* at 153:14–154:9, 204:12–23.) But that answer does not explain how Dr. Raines excludes centrally mediated nausea as a cause of delayed emptying when a patient’s GI symptoms are nausea and vomiting—the two symptoms Dr. Raines described as the “most prominent” for gastroparesis. (*Id.* at 93:16–22, 151:13–21; *id.* at 172:5–8 (agreeing that nausea and vomiting are the “key symptoms of gastroparesis”); *see also* May 14, 2025 Pt. 2 Tr. at 124:17–22 (Dr. Nguyen testifying that nausea and vomiting are “cardinal symptoms” of gastroparesis, meaning “you have to have those symptoms to diagnose gastroparesis but it doesn’t mean that those symptoms are pathognomonic of gastroparesis”).) Nor does Dr. Raines state that he can assume delayed emptying only when the patient’s symptoms also include bloating and abdominal pain.<sup>25</sup>

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In sum, Dr. Raines has not shown his assumption that symptoms and timing are reliable indicators of delayed gastric emptying is based on “good grounds.” It represents, at most, a hypothesis which has not yet been subjected to the rigors of science. *See In re Paoli*, 35 F.3d at 763–64 (“Presumably, Dr. DiGregorio’s general reasoning was that all of the plaintiffs had significant exposure to PCBs, that PCBs are a known cause of the illnesses of the various plaintiffs, and that, in the absence of any indication that any plaintiff had been exposed to something more likely to cause his or her illness than PCBs, it was reasonable to conclude that PCBs were a likely cause. But Dr. DiGregorio did not point to any evidence showing that PCB exposure was so likely to produce the type of illnesses the plaintiffs had in comparison to other

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<sup>25</sup> And, as discussed in the next subsection, even in patients that experience bloating and abdominal pain, Dr. Raines has not shown that he can reliably find the patient’s symptoms are caused by delayed gastric emptying as opposed to functional dyspepsia.



possible causes to which plaintiffs had likely been exposed that it was reliable to conclude that PCBs were the cause without further analysis. We think that the district court essentially, and properly, read Dr. DiGregorio's testimony as showing that his opinion that PCBs caused plaintiffs' illnesses was only a hypothesis which he had yet to attempt to verify or disprove by subjecting it to the rigors of scientific testing."); *Feit*, 460 F. Supp. 2d at 641 ("In the absence of any objective medical findings regarding head or neck injury, and without any analytical framework that would render the theory of possible head and neck injury a significant probability, let alone an uncontrovertible conclusion, Dr. Duong's opinion that Dr. Feit died of a head or neck injury is pure speculation, devoid of any discernible evidence or scientific method. Dr. Duong's conclusion that head or neck injury caused Dr. Feit's death is categorically a net opinion, a theory connected to existing data only by the ipse dixit of the expert." (quotation marks omitted)).<sup>26</sup> Accordingly, Dr. Raines's proposed differential diagnosis is excluded as unreliable to the extent it rests on this assumption.

*b. Alternative Diagnosis of Functional Dyspepsia*

In addition to challenging the assumptions of delayed gastric emptying underlying Dr. Raines's proposed methodology, Defendants also argue that his methodology is not based on

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<sup>26</sup> The Court also questions whether Dr. Raines's assumption about symptoms plus timing fits the issues in this case. When pressed to explain the type of patient for which he would find symptoms plus timing indicative of delayed emptying, Dr. Raines referenced the "classic case": "[A] patient with no history of any other illness, especially like no other like pre-existing symptoms, completely asystematic [sic], no medical problems, not on any other medicines, that suddenly started a drug, like a GLP-1, and then developed severe nausea and vomiting, with vomiting food within four hours after ingestion, that was kind of persistent for more than seven days or recurrent over the course of seven days." (Raines Dep. Tr. at 115:7–116:6; *see also id.* at 107:9–108:4 (describing "classic presentation"); May 14, 2025 Pt. 1 Tr. at 78:22–79:3 ("For patients that come to my clinic that have no diagnostic testing, no complicated medical history or known confounding factors, no signs or symptoms of any other pathology, I make that diagnosis in clinic if their history is consistent with drug-induced gastroparesis and there's no indicators of any other pathology.")). But every Plaintiff in this MDL is expected to have a "history of . . . other illness," and indeed, will likely be on "other medicines," because GLP-1 RAs are indicated only for patients who suffer from Type 2 diabetes and/or obesity.

“good grounds” because it fails to account for the possible alternative diagnosis of functional dyspepsia. *See In re Paoli*, 35 F.3d at 760–62 (explaining that a physician’s differential diagnosis may be found unreliable when the defendants has “pointed to some likely [alternative] cause of the plaintiff’s illness” and the physician has failed to offer a “good explanation as to why their conclusion remained reliable”). The Court agrees that Dr. Raines has not provided a “good explanation” as to how he can reliably find a patient is suffering from gastroparesis as opposed to experiencing symptoms of functional dyspepsia.

Functional dyspepsia is defined as “the presence of one or more of the following symptoms: bothersome postprandial fullness, bothersome early satiation, bothersome epigastric pain, or bothersome epigastric burning, and no evidence of structural disease . . . to explain the symptoms.” *Blurring*, at 28. Functional dyspepsia and gastroparesis represent the two most common sensorimotor disorders of the stomach. *See Misdiagnosis* at 2670. The two disorders have similar symptom presentations and are “usually confused,” such that “numerous patients [are] mistakenly labeled as having [gastroparesis]” when the more accurate diagnosis is functional dyspepsia. *Blurring* at 27; *see also, e.g., 2025 Rome Consensus* at 69 (“Symptoms associated with delayed gastric emptying could also be associated with other gastroduodenal function alterations (e.g., functional dyspepsia), which could contribute to the inconsistent relationship between symptom pattern and severity and a delay in gastric emptying.”); *Misdiagnosis* at 2671 (finding “no difference in symptom presentation between” the group of patients ultimately diagnosed with gastroparesis and those diagnosed with functional dyspepsia); Hiroki Sato & Madhusudan Grover, *Gastroparesis and Functional Dyspepsia: Spectrum of Gastroduodenal Neuromuscular Disorders or Unique Entities?*, 2 *Gastro Hep Advances* 438, 438 (2023) (filed as Doc. No. 359-3 at Ex. N) (“The clinical presentation and treatment of

gastroparesis overlap with a more commonly recognized disorder of gut-brain interaction, functional dyspepsia. . . . Recent studies have highlighted a substantial overlap in the pathophysiology, symptoms, and clinical course of gastroparesis and [functional dyspepsia].”); *id.* at 439 (noting that some studies “suggest a significant overlap and lack of symptoms specific for the two disorders”); (May 14, 2025 Pt. 2 Tr. at 101:3–4 (Dr. Nguyen testifying that “symptoms alone cannot help differentiate gastroparesis from functional dyspepsia”)).

When asked about functional dyspepsia, and in particular, the subset of functional dyspepsia known as postprandial distress syndrome, Dr. Raines agreed that it, like gastroparesis, is “characterized by upper epigastric pain or discomfort, bloating, and fullness.” (May 14, 2025 Pt. 1 at 172:9–17.) He also agreed that “[i]f the primary symptom is abdominal pain, the diagnosis of gastroparesis should be questioned, particularly if there is chronic dependence on opioids.” (*Id.* at 172:18–24.) When asked how, given this, he would distinguish functional dyspepsia from gastroparesis without a gastric emptying study, he stated that he would look for evidence that the patient had been suffering from GI complaints their whole life. (*Id.* at 34:21–35:20.) But neither he nor Plaintiffs have shown this method for distinguishing between functional dyspepsia and gastroparesis has been tested, is generally accepted in the medical community, or has a known error rate. Indeed, in all the literature submitted by the parties, the Court found no suggestion that this is a recognized method for distinguishing the two disorders.

Dr. Raines’s failure to account for this probable alternative diagnosis further suggests his proposed methodology is not a reliable method for diagnosing gastroparesis. *See Kannankeril*, 128 F.3d at 808 (“In attacking the differential diagnosis performed by the plaintiff’s expert, the defendant may point to a plausible cause of the plaintiff’s illness other than the defendant’s actions. It then becomes necessary for the plaintiff’s expert to offer a good explanation as to

why his or her conclusion remains reliable.”); *see also Heller*, 167 F.3d at 159 (finding the district court could “properly consider Dr. Papano’s (weak) responses to Shaw’s proffered alternative theories on the cause of Heller’s illness in evaluating whether he truly had ‘good grounds’ to arrive at the causation conclusion he reached.”); *Hoefling*, 576 F. Supp. 3d at 275 (“Alternatively, Dr. Busse’s view is not scientific because it is mere subjective belief propped up by biological plausibility rather than an objective inference from the relevant scientific evidence—which does not draw the necessary causal connection between Defendants’ smokeless tobacco products and tonsil cancer.” (quotation marks omitted)).

#### 4. Conclusion

In conclusion, Dr. Raines’s differential diagnosis is not reliable. He opines that before a physician can diagnose a patient with drug-induced gastroparesis, they must find the patient suffers from delayed gastric emptying. He identifies two methods for finding that requirement satisfied in the absence of a gastric emptying study: (1) symptoms plus timing, or (2) evidence of retained gastric food. But neither method is recognized as a standard diagnostic technique for measuring gastric emptying or diagnosing gastroparesis, and Dr. Raines has not otherwise shown that these methods are reliable. Accordingly, Dr. Raines’s overarching conclusion that a physician can diagnose gastroparesis without a gastric emptying study is also not reliable and is excluded. *See In re Silica Prods. Liab. Litig.*, 398 F. Supp. 2d 563, 625 (S.D. Tex. 2005) (“Looking no further than the first criterion, virtually all of the diagnoses fail to satisfy the minimum, medically-acceptable criteria for the diagnosis of silicosis, and therefore, the testimony of the challenged doctors cannot be admissible under the standards set by Rule 702 and *Daubert*.”).

### C. Dr. Siegel

Next, Defendants move to exclude Plaintiffs’ remaining expert, Dr. Siegel. They challenge Dr. Siegel’s qualifications as well as the reliability of his opinions.

#### 1. Dr. Siegel’s Qualifications

First, Defendants argue that Dr. Siegel is not qualified to offer an opinion on how to reliably diagnose gastroparesis because he has no formal training in gastroenterology or internal medicine, let alone motility disorders. (Doc. No. 360-1 at 26–28; Doc. No. 361-1 at 23; May 19, 2025 Hr’g Tr. at 61:23–62:5, 69:2–3.) Defendants emphasize that Dr. Siegel has never assigned a diagnosis of *drug-induced* gastroparesis, has never employed the methodology he advocates for in this case, and much of his report is based on an incomplete literature review that he performed solely for this litigation. The Court shares many of Defendants’ concerns. (See May 14, 2025 Pt. 2 Tr. at 64:1–13 (Dr. Siegel testifying that portions of the report “go outside of [his] expertise,” and that he is “not an expert on gastroenterology in general,” just an “expert on gastroenterology as it applies to medical imaging”).) That said, we find these issues go to the reliability of Dr. Siegel’s expert opinions; they do not render him entirely unqualified to give those opinions. See *In re Paoli*, 35 F.3d at 741 (“As we explain below . . . the level of expertise may affect the reliability of the expert’s opinion.”).

As noted previously, the Third Circuit liberally interprets Rule 702’s qualifications requirement and has “eshewed imposing overly rigorous requirements of expertise.” *Id.* “[A] broad range of knowledge, skills, and training qualify an expert as such,” *id.*, and it is an “abuse of discretion to exclude testimony simply because the trial court does not deem the proposed expert to be the best qualified or because the proposed expert does not have the specialization that the court considers most appropriate,” *Holbrook v. Lykes Bros. S.S. Co.*, 80 F.3d 777, 782 (3d Cir. 1996); accord *Pineda*, 520 F.3d at 244.

*In re Paoli* is instructive. In that case, the district court found one of the plaintiffs' expert physicians unqualified to offer an opinion as to whether PCBs caused the plaintiffs' adverse health effects. 35 F.3d at 753. In excluding the expert, the district court emphasized that she "no longer practice[d] general internal medicine," "lack[ed] board certification in any medical specialty including internal medicine and toxicology," and during her expert testimony, "made numerous basic medical errors in the fields of immunology, internal medicine and dermatology." *Id.* On appeal, the Third Circuit reversed. The appellate court found that "while arguably a relatively poor clinician and less than fully credible witness," the doctor "qualifie[d] as an expert." *Id.* The court noted that the doctor served on the consulting staff of a hospital for many years, and after leaving had "extremely broad experience in the field of toxic substances," writing "extensively in the field." *Id.* And although she "made substantive mistakes in her testimony," that same testimony also "demonstrated significant familiarity with the literature on PCBs." *Id.* at 754. Given her experience, the court found she satisfied the "liberal standards for qualifications of experts." *Id.* (reasoning that Rule 702 "surely allows a trained internist who has spent significant time reviewing the literature on PCBs to testify as to whether PCBs caused illness in plaintiffs"); *see also Holbrook*, 80 F.3d at 782 ("The court's mistaken approach restricted Dr. Carpenter's testimony based on a requirement that the witness practice a particular specialty to testify concerning certain matters. In light of our liberal standard governing the qualifications of a proffered expert witness, and our acceptance of more general qualifications, we hold that the district court erred by finding that Dr. Carpenter was not qualified to render a diagnosis or to discuss the pathology report because he was not a pathologist, oncologist or expert in 'definitive cancer diagnosis.'").

Here, the Court finds that even if Dr. Siegel is not the most qualified expert, he is nevertheless sufficiently qualified to opine about diagnosing gastroparesis, and in particular, the role that nuclear medicine and imaging studies play in that diagnosis. Dr. Siegel is a board-certified radiologist with over 37 years of experience. (Siegel Rpt. at 3.) During that time, he served as the Chief of Diagnostic Radiology and Nuclear Medicine at the VA Maryland Healthcare System and as a tenured professor at the University of Maryland. (*Id.*; *see also* May 14, 2025 Pt 2 Tr. at 6:7–22, 7:13–8:7.) He has interpreted tens of thousands of nuclear medicine examinations, including more than 2,000 gastric emptying studies, in addition to CT scans, MRIs, and other imaging studies. (*See* May 14, 2025 Pt 2 Tr. at 12:18–13:1.) Dr. Siegel has also interpreted the presence or absence of mechanical obstruction via CT scans and upper GI imaging on thousands of occasions and reported the presence of retained food and gastric distension, gastric wall thickening, and gastric masses on CT scans in thousands of cases. (Siegel Rpt. at 5.) In addition to performing and reviewing these various studies, Dr. Siegel has also personally diagnosed gastroparesis on at least 100 occasions. (*Id.*) And he attests that he has consulted with primary care physicians about the appropriate diagnosis and treatment of patients, including patients experiencing distension or whose studies reveal evidence of retained gastric food. (*Id.*)

Although Dr. Siegel testified that portions of his report were based purely on a literature review that he conducted solely for this litigation (*see* Siegel Dep. Tr., Doc. No. 360-8, at 277:16–278:9; May 14, 2025 Pt. 2 Tr. at 62:10–63:12), he clarified that his ultimate opinions are also based on this extensive experience (*see* May 14, 2025 Pt. 2 Tr. at 63:25–64:8). *See Schneider ex rel. Estate of Schneider*, 320 F.3d at 406 (“In the case at bar, Dr. Semigran stated that he based his opinion not only upon the literature, but also upon his own experience as a

cardiologist.”); *cf. In re TMI Litig.*, 193 F.3d 613, 680 (3d Cir. 1999) (“So far as the record is concerned, his *only* knowledge of the health effects of radiation was obtained from literature he reviewed in connection with his retention as an expert in this litigation. He plainly does not meet Rule 702’s ‘Qualifications’ requirement and cannot, therefore, offer an expert opinion as to radiation induced medical conditions.” (emphasis added)).

Given Dr. Siegel’s experience diagnosing gastroparesis and conducting the very studies that lie at the heart of Cross Cutting Issue No. 1, the Court cannot find Dr. Siegel *unqualified* to offer the opinions he puts forth in this case. *See In re: Zostavax*, 579 F. Supp. 3d at 678 (“While he has no experience with patients who have been inoculated with Zostavax, his experience and formal qualifications are sufficient to meet the less than stringent standards to qualify as an expert here.”). Nevertheless, Dr. Siegel’s lack of experience diagnosing drug-induced gastroparesis or using his proposed methodology certainly affects the reliability of his opinions and thus is considered in the next section.

## 2. The Reliability of Dr. Siegel’s Opinions

Like Dr. Raines, Dr. Siegel opines that no objective testing of delayed gastric emptying is required for a physician to reliably diagnose drug-induced gastroparesis. (*See* Siegel Dep. Tr. at 125:4–9, 200:4–18; *see also id.* at 296:21–23 (describing his opinion as “one can diagnose gastroparesis based on the temporal relationship of a medication and also GI symptoms”); May 14, 2025 Pt. 2 Tr. at 79:21–80:3 (agreeing with statement in his report that “where induction or titration of medication known to cause delayed gastric emptying is temporally related to the classic symptoms of gastroparesis, a diagnosis can be made without the need to order a gastric emptying study or other imaging”).) Dr. Siegel also opines that to the extent objective evidence of delayed gastric emptying is needed, a physician does not need to have performed one of the



three gastric emptying tests identified by Defendants. He notes that alternative studies—including x-rays, ultrasounds, CT scans, MRIs, and barium upper GI series—can provide evidence of distension and retained gastric food, which suggest delayed emptying. (*See* May 14, 2025 Pt. 2 Tr. at 25:17–30:7.)

Defendants argue that Dr. Siegel’s primary opinion is unreliable for the same reasons Dr. Raines’s identical opinion is unreliable. (Doc. No. 360-1 at 22–26; Doc. No. 361-1 at 18–23; May 19, 2025 Hr’g Tr. at 69:3–14.) They also move to exclude his opinion that other tests can provide reliable evidence of delayed gastric emptying. (*See* May 19, 2025 Hr’g Tr. at 69:3–14, 180:6–14.) Defendants argue that although a variety of tests may assist in the evaluation of a patient, only three tests can reliably establish the presence of delayed gastric emptying—scintigraphy, breath testing, and WMC. The Court agrees with Defendants.

*a. Symptoms Plus Timing*

Dr. Siegel, like Dr. Raines, opines that a physician can reliably find delayed gastric emptying where the patient experiences upper GI symptoms after initiating or titrating a GLP-1 RA. (*See* Siegel Dep. Tr. at 72:1–74:13, 102:17–25.) As the Court previously found, this opinion is contrary to standard diagnostic techniques, and Dr. Siegel has not otherwise shown that it is a reliable methodology for finding delayed emptying. He has not tested his methodology, cannot identify where others have tested the methodology, and—as noted in connection with Dr. Raines—the literature on the issue does not support the methodology. (*See* Siegel Dep. Tr. at 127:9–128:9, 259:5–261:10; *cf.* Siegel Dep. Tr. at 292:21–293:5 (conceding that three studies referenced in his report “call into question whether the presence of symptoms can be used to predict delayed gastric emptying”).) Nor has Dr. Siegel shown that he has accounted for alternative probable diagnoses like central mediated nausea and functional

dyspepsia. To the contrary, when asked at his deposition how he determines “in an individual case that the effect [he is] seeing is related to the gastric emptying effect of the medication as opposed to something else,” like central mediated nausea, Dr. Siegel responded that the question was “outside the scope of [his] report.” (Siegel Dep. at 253:5–23.) Indeed, although Dr. Raines requires the presence of symptoms for at least seven days to rule out other diagnoses like gastroenteritis, Dr. Siegel has no such requirement. (*See* May 14, 2025 Pt. 2 Tr. at 57:17–23.)

Accordingly, the Court finds unreliable Dr. Siegel’s opinion that symptoms plus timing is a reliable indication of delayed gastric emptying.

*b. Alternative Tests*

That leaves Dr. Siegel’s opinions about alternative testing. He opines that a gastric emptying study is not required because physicians can find delayed emptying using other studies, including x rays, CT scans, MRIs, ultrasounds, and upper GI series (sometimes referred to as a “barium swallow”). (*See* Siegel Rpt. at 13–14; May 14, 2025 Pt. 2 Tr. at 25:17–27:13.) Defendants argue that this portion of Dr. Siegel’s opinion is also unreliable because it is contrary to the standard diagnostic techniques accepted in the medical field and Dr. Siegel has not otherwise shown these tests reliably measure gastric emptying.<sup>27</sup> The Court agrees.

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<sup>27</sup> Plaintiffs argue that Defendants have not challenged this opinion by Dr. Siegel. (May 19, 2025 Hr’g Tr. at 163:11–15.) But that argument is somewhat disingenuous given the evolution of Dr. Siegel’s opinions in this case. Notably, although Dr. Siegel mentioned each of these tests in his expert report, his opinion at that stage of the proceedings was limited to the assertion that “[i]maging, endoscopy, or a GES can provide an additional datapoint for the diagnosis of GLP-1 RA-induced gastroparesis *but is usually not necessary*.” (Siegel Rpt. at 26 (emphasis added).) When Defendants challenged this opinion in their briefing, they understandably focused on Dr. Siegel’s assertion that objective testing was “not necessary”—not on the unspoken conclusion that the “imaging” studies referenced above could provide objective evidence of delay. Accordingly, this issue took up only a small portion of the parties’ briefing and Dr. Siegel’s deposition. It was only at the evidentiary hearing that Dr. Siegel changed course and explicitly opined that these tests are reliable—and “objective”—alternatives for measuring gastric emptying. At the hearing, that opinion was the focus of Dr. Siegel’s direct examination. And Defendants certainly challenged it at that stage, both on cross-examination and during oral argument. (*See* May 14, 2025 Pt. 2 Tr. at 47:3–48:14, 68:25–69:6, 83:12–85:20; May 19, 2025 Hr’g Tr. at 69:3–14, 180:6–14.) Because Defendants have challenged the substance of this portion of Dr.

First, Defendants are correct that none of these alternative tests are considered a standard diagnostic technique for measuring delayed emptying. Instead, the medical literature is unanimous in recognizing a properly performed scintigraphy study is the “gold standard” for measuring gastric emptying. *See, e.g., 2020 UEG & ESNM Consensus* at 294; *see also 2022 ACG Guideline* at 1200–02 (“SGE [scintigraphy] is the standard test for the evaluation of GP in patients with upper GI symptoms.”). And breath testing and WMC are the recognized alternatives to scintigraphy. *See, e.g., 2022 ACG Guideline* at 1200–02 (“WMC testing may be an alternative to the [scintigraphy] assessment for the evaluation of GP. . . . Stable isotope (<sup>13</sup>C-spirulina) breath test is a reliable test for the evaluation of GP.”); *2020 UEG & ESNM Consensus* at 294 (endorsing breath test as “valid” for “diagnosing gastroparesis”); *N. Am. Perspective* at 4 (agreeing with “the endorsements by the ESNM working group regarding the diagnosis of gastroparesis,” including the group’s endorsement of “gastric emptying testing (by scintigraphy or breath test)” as “mandatory for establishing a diagnosis of gastroparesis”); *Blurring*, at 30–31 & Tbl. 2 (recognizing breath test, and WMC as “reasonable modalities for the estimation of [gastroparesis]” and identifying those two, plus scintigraphy, as the only “methods used to assess gastric emptying”). This lack of general acceptance weighs against the reliability of Dr. Siegel’s opinions. *See In re TMI Litig.*, 193 F.3d at 669 (“[A] court may well cast a jaundiced eye upon a technique which is not supported by any evidence of general acceptance absent other indicia of reliable methodology.”).

Dr. Siegel testified that his alternative testing methods are nevertheless reliable because he can use those modalities to identify the presence of retained gastric food and/or distension of

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Siegel’s opinion, the Court will not consider it uncontested merely because it does not appear in Defendants’ briefing.

the stomach caused by retained food or liquid. (See May 14, 2025 Pt. 2 Tr. at 29:21–30:6; see also *id.* at 25:17–26:5 (testifying that “computed tomography[,] ultrasound, conventional x-rays, upper GI series, [and] magnetic resonants [sic] imaging” are capable of “identifying food contents that are undigested”); *id.* at 27:10–13 (“[D]istention represents an increase in the volume of the stomach, in this case, the stomach and we have the capabilities of visually seeing that a stomach is distended or has a greater volume of content than it does normally. I also have the capabilities on CT and on ultrasound and on x-ray and on MRI to be able to make measurements to be able to determine the degree of distention and indirectly try to estimate the volume of distention as well from those studies.”).) But as discussed previously in connection with Dr. Raines’s opinions, the presence of retained gastric food is explicitly rejected by the medical community as a reliable indicator of delayed gastric emptying. See *supra* Part III.B.3.b. It follows that the modalities that measure retained gastric food are, by extension, unreliable.<sup>28</sup> Likewise, modalities that measure distension, appear even less reliable because, as Dr. Nguyen testified, things besides retained gastric food may cause distension, including residual liquids and air. (May 14, 2025 Pt. 2 Tr. at 111:19–112:1.)

Dr. Siegel testified that in addition to measuring retained food and distension, ultrasound and barium swallow can be used to measure gastric emptying. He notes that an ultrasound “can be done repeatedly over the course of an individual’s visit to a hospital,” so that the radiologist

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<sup>28</sup> This conclusion is limited to the ability of these tests to reliably measure gastric *emptying*. Given the limited scope of Cross Cutting Issue No. 1, the Court need not address whether these modalities are able to reliably rule out gastric outlet obstruction or assess gastric *accommodation*. See, e.g., Ghazanfar, et al., *Diagnostic Modalities 2022*, at 2 (discussing esophagogastroduodenoscopy, double-contrast upper gastrointestinal radiography, CT enterography, and magnetic resonance enterography as “tests that help rule out a mass, ulcer, or stricture present in the gastrointestinal tract”); *Blurring 2019* at 31 (“Newly developed techniques such as single-photon emission computed tomography, 3-dimensional ultrasonography, and magnetic resonance imaging can measure gastric volumes and are promising alternatives for the noninvasive assessment of gastric accommodation.”).

can see the rate at which fluid and solid material are moving out of the stomach. (*Id.* at 28:19–29:1.)<sup>29</sup> Similarly, in a “barium swallow . . . as is the case with ultrasound, but to a greater extent, [the physician] can follow the dynamic kinetics associated with the flow of the barium through the esophagus into the various portions into the stomach and duodenum,” which allows them to “visualize the contraction of the stomach directly” and “the rate and speed during a period of perhaps 10 to 20 minutes of clearance from the esophagus and from various aspects of the stomach and into the small bowel.” (*Id.* at 26:19–21; 27:18–28:8.)

But again, Dr. Siegel has not put forth any evidence to suggest these modalities, which are not standard diagnostic techniques, provide *reliable* measurements of gastric emptying. Dr. Siegel could not identify any literature to support his use of these modalities to measure delayed emptying. (*Id.* at 43:15–19.) And to the limited extent the literature discusses this issue, it suggests neither ultrasound nor barium swallow are generally accepted by the medical community as modalities for measuring gastric emptying. Many of the consensus documents and guidelines question the reliability of using an ultrasound to measure gastric emptying, noting it has “proven reliable only for measurements of liquid emptying rates,” is “operator dependent,” and “difficult” to perform “in obese individuals.”<sup>30</sup> Henry P. Parkman et al., *American Gastroenterological Assoc. Tech. Review on the Diagnosis & Treatment of Gastroparesis*, 127 *Gastroparesis* 1592, 1597 (2004) (filed as Doc. No. 360-12) (“2004 AGA Review”); *see also* 2025 Rome Consensus at 71 (“Gastric ultrasonography . . . is unsuitable to

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<sup>29</sup> Dr. Siegel suggested that a CT scan can similarly be repeated, but he went on to testify that “in actual practice that isn’t done,” so the Court does not consider him to be opining that physicians consistently and reliably use multiple CT scans to measure the rate of emptying. (*See* May 14, 2025 Pt. 2 Tr. at 32:20–33:1.)

<sup>30</sup> As a reminder, obesity is an indication for many of the GLP-1 RAs at issue in this litigation, and it is reasonable to presume that some portion of Plaintiffs will have been suffering from obesity when they were given a diagnosis of gastroparesis.

assess the emptying of solids, requires an experienced technician, is user dependent, could be influenced by the presence of intragastric air or posture, and is generally considered impractical for longterm observations.”); *2020 UEG & ESNM Consensus* at 294 (declining to endorse gastric ultrasound as “valid” for “diagnosing gastroparesis”); *N. Am. Perspective* at 4 (“We agree with the endorsements by the ESNM working group regarding the diagnosis of gastroparesis, specifically . . . gastric emptying testing (by scintigraphy or breath test, but not by wireless motility capsule *or ultrasound*) being mandatory for establishing a diagnosis of gastroparesis . . . .” (emphasis added)). Similarly, the *2004 AGA Review*—the only guideline document or journal article that the Court found to discuss the reliability of barium swallow—states that although a barium swallow may produce results “suggestive of gastroparesis,” it is ultimately “an insensitive method for measuring gastric emptying because it is difficult to quantitate the relative fraction of contrast delivered to the intestine and because barium is not a ‘physiologic’ test meal.” *2004 AGA Review* at 1594; *see also HHS Review* at 2 (“Additional methods of evaluation (e.g., upper gastrointestinal [GI] endoscopy, computed tomographic enterography, magnetic resonance enterography, or barium follow-through examination) can assist in determining the presence of mechanical obstruction or food retention after an overnight fast; however, these evaluations do not assess gastric motility and the presence of retained food is considered supportive but not diagnostic for [gastroparesis].”).<sup>31</sup> Dr. Siegel has not acknowledged or accounted for any of these concerns. *See In re Rezulin Prods. Liab. Litig.*, 369 F. Supp. 2d 398, 425 (S.D.N.Y. 2005) (“[I]f the relevant scientific literature contains evidence

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<sup>31</sup> Dr. Nguyen, who is a coauthor of the *2022 ACG Guideline* and the *2025 Rome Consensus*, testified that the guidelines do not recommend using these modalities because they can’t control for possible confounders, i.e., “things that may delay gastric emptying that’s not related to the diagnosis of gastroparesis.” (May 14, 2025 Pt. 2 Tr. at 109:16–21.) She explained that when a physician performs “endoscopy or CT scan or barium study” they can’t “control for those confounders.” (*Id.*)

tending to refute the expert’s theory and the expert does not acknowledge or account for that evidence, the expert’s opinion is unreliable.”).

In addition to lacking general acceptance in the field, Dr. Siegel testified that he has not tested the reliability of using his methodology to measure delayed emptying, nor has he identified the potential error rate associated with using either ultrasound or barium swallow to measure delayed emptying. (May 14, 2025 Pt. 2 Tr. at 53:9–17; 54:21–24.) He has not published his proposed methodology or sought peer review from other experts in the medical field. (*Id.* at 51:23–52:16.) And, tellingly, Dr. Siegel has never diagnosed a patient with gastroparesis using either method.<sup>32</sup> (*See id.* at 44:9–25, 70:21–24; Siegel Dep. Tr. at 199:11–16); *see also Kumho Tire Co.*, 526 U.S. at 157 (“We have found no indication in the record that other experts in the industry use Carlson’s two-factor test or that tire experts such as Carlson normally make the very fine distinctions about, say, the symmetry of comparatively greater shoulder tread wear that were necessary, on Carlson’s own theory, to support his conclusions. Nor, despite the prevalence of tire testing, does anyone refer to any articles or papers that validate Carlson’s approach. . . . Indeed, no one has argued that Carlson himself, were he still working for Michelin, would have concluded in a report to his employer that a similar tire was similarly defective on grounds identical to those upon which he rested his conclusion here.”); *Soldo*, 244 F. Supp. 2d at 527 (“Expert opinions generated as the result of litigation have less

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<sup>32</sup> Although Dr. Siegel has diagnosed around 100 patients with gastroparesis, each of those patients had a gastric emptying scintigraphy study, which reflected delayed gastric emptying. (*See* May 14, 2025 Pt. 2 Tr. at 43:7–14; *see also id.* at 11:2–5 (testifying that “with the exception of about 100 patients” he “do[es]n’t diagnose gastroparesis”); *id.* at 11:6–25 (discussing the 100 patients).) *See In re Silica*, 398 F. Supp. 2d at 634 (criticizing “the idea that when doctors step into a courtroom, they can abandon the methodology they practice in the clinic”).

credibility than opinions generated as the result of academic research or other forms of ‘pure’ research.”).

Finally, as noted above, although the Court finds Dr. Siegel qualified, his qualifications are certainly somewhat suspect because he has *never* diagnosed a patient with drug-induced gastroparesis, nor has he diagnosed a patient with any subset of gastroparesis without a scintigraphy study. *See supra* n.32. Dr. Siegel’s limited qualifications in this area further weigh against a finding that his opinion is reliable. *See Rivlin v. Biomet*, Civil Action No. 19-1497-KSM, 2021 WL 3128672, at \*9 (E.D. Pa. July 23, 2021) (“This lack of study, peer review, or general acceptance is particularly telling in this case because Fruchter has only limited qualifications in weather forecasting.”).

Indeed, Dr. Siegel’s testimony at the evidentiary hearing and during his deposition suggest that portions of his opinion, including portions of his discussion about standard diagnostic techniques for gastroparesis, were solely based on a literature review that he conducted to prepare his report, as opposed to knowledge and methods he employs in his practice. (*See* Siegel Dep. Tr. at 277:16–278:9 (conceding that “this is the first time” he has “put together or written an opinion on the topic in this litigation,” and explaining that “[t]his litigation gave [him] the opportunity to do a fairly deep literature search that [he] had not done before in order to create this report”); *see also* May 14, 2025 Pt. 2 Tr. at 62:10–13 (“[M]uch of the information in the report is information from my review of the literature and a summary of what the literature states. That was the purpose of it. It was not to create my own opinions on these topics.”); *id.* at 63:1–12 (“[W]hen I was asked to do the report, I was not asked to provide my own personal opinions about this. What I did and what I was asked to do was create a summary of the information, the literature about that information.”).)



In addition to testifying that, at times, he relied solely on his literature review to form his opinions, Dr. Siegel also testified that he did not thoroughly read all the literature on which his opinions are based. (*See* Siegel Dep. Tr. at 279:21–280:14 (“So in the Materials Considered, I looked at all of the materials—all of the articles I included in Materials Considered in detail. But I—a subset of those articles I may not have read every single section, but I tried to find all the sections in those articles that I thought were relevant to my report, plus ones that I was curious about that weren’t necessarily in the report.”); *id.* at 297:3–11 (clarifying that for those studies which he considered relevant, he “read the parts of those studies that [he] thought were most relevant to the assignment in the report in detail. But there is no doubt in [his] mind that there are portions of what [he] read that [he] did not believe necessarily related to [his] report and that [he] didn’t read”); *id.* at 297:22–298:5 (“In other words, I don’t know what I didn’t read. . . . There were sections that were labeled. Sometimes I might have read an abstract. In some cases, it’s possible that there was an abstract that I didn’t have the full text to and just relied on the abstract.”).)

Dr. Siegel’s substantive opinions also frequently changed between his report, his deposition testimony, and his testimony during the evidentiary hearing. (*See, e.g.,* Siegel Dep. Tr. at 135:22–138:5 (changing portions of his report); May 14, 2025 Pt. 2 Tr. at 61:1–67:5 (testifying that he does not agree with the portion of his report where he said non-drug-induced gastroparesis should be confirmed with a gastric emptying study); *id.* at 77:10–81:14 (reviewing the portion of his report where he stated that neither a gastric emptying study nor imaging studies are required to diagnose gastroparesis, including imaging to rule out mechanical blockage, and testifying that although technically correct, he believes “one should perform imaging to evaluate for the possibility of mechanical obstruction”).)

Two instances are particularly noteworthy as they go to the heart of his opinion that the alternative tests are reliable modalities for determining whether a patient suffers from delayed gastric emptying. First, when Dr. Siegel was presented at the evidentiary hearing with the portion of his deposition testimony where he described x-ray, CT scan, MRI, and barium swallow as “subjective” tests, he stated that he was “changing” his testimony to say that all four tests are actually “objective.” (May 14, 2025 Pt. 2 Tr. at 47:7–48:14.) Whether those tests are “subjective” or “objective” is relevant because the guidelines call for “*objective* evidence of delayed gastric emptying.” *See, e.g., 2022 ACG Guideline* at 1197 (“Gastroparesis (GP) is a motility disorder characterized by symptoms and *objective documentation* of delayed gastric emptying (GE) of solid food without mechanical obstruction . . . .” (emphasis added)). Second, when reviewing the portion of his report which states, “When faced with suspected drug-induced gastroparesis, *I go about* evaluating whether the diagnosis is appropriate in a number of ways,” Dr. Siegel conceded that he had never been “faced with suspected drug-induced gastroparesis” and that his report should be changed to state, “*if I were faced with* suspected drug-induced gastroparesis, these would be the things that I would do.” (May 14, 2025 Pt. 2 Tr. at 67:9–68:24 (emphases added).)

These and other discrepancies call into question Dr. Siegel’s credibility in reaching his opinion about alternative tests, as well as the other opinions that he gives in his expert report and related testimony. *See Elcock v. Kmart Corp.*, 233 F.3d 734, n.8 (3d Cir. 2000) (“[U]nder certain circumstances, a district court, in order to discharge its fact-finding responsibility under Rule 104(a), may need to evaluate an expert’s general credibility as part of the Rule 702 reliability inquiry.”); *cf. id.* (“For instance, . . . at least one prominent evidence commentator has noted that . . . a court should take [the expert’s] dishonesty or misconduct into account when the

nexus between the acts and expert’s methodology is more direct. . . . Under this approach, for instance, the fact that an expert witness falsely reported his salary on an income tax return has little if any bearing on the reliability of a diagnostic test he frequently employs, but the fact that the expert lied about whether his methodology had been subjected to peer review, or intentionally understated the test’s known rates of error, is a different matter entirely.”).

These credibility concerns support the Court’s reliability analysis under *Paoli* and the Court’s ultimate conclusion that Dr. Siegel’s opinion about alternative testing is unreliable.<sup>33</sup>

### 3. Conclusion

In sum, Dr. Siegel’s proposed methods for measuring delayed emptying are not reliable. He, like Dr. Raines, opines that before a physician can diagnose a patient with drug-induced gastroparesis, there must be evidence of delayed gastric emptying. He identifies two methods for finding that requirement satisfied in the absence of a gastric emptying study: (1) where the patient has symptoms plus timing, (2) where an alternative test shows evidence of retained gastric food and/or distension, or, in the context of an ultrasound or barium swallow, suggests delayed emptying. But none of these methods is recognized as a standard diagnostic technique for measuring gastric emptying or diagnosing gastroparesis, and Dr. Siegel has not shown that they are otherwise reliable. Accordingly, Dr. Siegel’s opinions are not reliable and excluded.

### **D. Dr. Nguyen**

Last, Plaintiffs move to exclude two opinions issued by Dr. Nguyen. First, they move for exclusion of her opinion that “drug-induced or physiologic gastroparesis” is not “true” gastroparesis. (Doc. No. 359-1 at 8–13.) Defendants oppose the motion, arguing that this is not

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<sup>33</sup> Even if the Court had found Dr. Siegel to be a credible witness, we would nevertheless find his opinions on alternative testing unreliable given our reliability analysis under *Paoli*.

an opinion Dr. Nguyen is offering at this time, and even if she were, they have no intention of relying on it. (Doc. No. 377 at 8–9.) During the evidentiary hearing, Dr. Nguyen confirmed that it is her “opinion that [GLP-1 RAs] *can* cause drug-induced gastroparesis.” (May 14, 2025 Pt. 2 Tr. at 123:19–23 (emphasis added).) Given this testimony and Defendants’ assertions, Plaintiffs’ first challenge is moot, and the Court does not address it further.

Second, Plaintiffs move to exclude Dr. Nguyen’s opinion that “[w]hile GI symptoms are quite common with GLP-1 RAs, clinically delayed gastric emptying is relatively rare.” (Doc. No. 359-1 at 13–14 (discussing Nguyen Rpt. at 17).) Plaintiffs argue that this opinion is not reliable because Dr. Nguyen cites only a single unpublished abstract—which we will refer to as the “*Lupianez-Merly Abstract*”—in support of her conclusion, and she did not conduct a literature review about GLP-1 RAs or their effect on gastric emptying. (Doc. No. 359-1 at 13–14.) Defendants argue that this mischaracterizes Dr. Nguyen’s opinion, which was issued to rebut Plaintiffs’ experts’ opinions that symptoms plus timing can alone be evidence of delayed gastric emptying. (Doc. No. 377 at 9–13.) They also note that the *Lupianez-Merly Abstract* was cited by both of Plaintiffs’ experts, and regardless, Plaintiffs have not put forth data or conclusions contrary to those presented in the abstract. (*Id.* at 9–10.)

As the *Lupianez-Merly Abstract* is the focus of the parties’ dispute, it is worth discussing in some detail. Because it has been submitted only in abstract form,<sup>34</sup> however, the Court has only a basic overview of the authors’ study. *See* Camille Lupianez-Merly et al., *Effects of GLP-1 Receptor or Dual GLP-1/GIP Receptor Agonists on Gastrointestinal Symptoms and Gastric Emptying: Results from a Large Clinical Practice Database*, AGA Abstracts, at S-1066–67

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<sup>34</sup> Defendants have also submitted a conference poster that discusses the study (*see* Doc. No. 360-3), but the poster provides little more detail than the abstract and was not referenced as a basis for Dr. Nguyen’s opinion, so the Court focuses on the abstract.

(2024) (filed as Doc. No. 359-3 at Ex. S) (“*Lupianez-Merly Abstract*”). According to the abstract, the authors reviewed the health records for around 80,000 patients on the Mayo Clinic Platform who had been prescribed a GLP-1 RA or dual GLP-1 RA/GIP RA. *Id.* at S-1066. The authors found that 14,658 patients developed at least one symptom suggestive of gastroparesis, and 3,993 developed at least two symptoms. *Id.* Among those, who had at least one symptom, “696 underwent validated [scintigraphy], of which 35% (241/696) had delayed [gastric emptying] at 4hr.” *Id.* Of those 241 patients, 127 had preexisting GI symptoms and 38 had documentation of a prior delayed [scintigraphy].” *Id.* at S-1066–67. The authors note that “[t]he distribution of GI symptoms among those with and without delayed [gastric emptying] was similar except for constipation which was more common in those with delayed [gastric emptying].” *Id.* at S-1067. According to the authors, “[t]hese real world data suggest that GI symptoms are prevalent in those treated with GLP-RA. However, not all these patients had impaired [gastric emptying]; symptoms likely represent a spectrum of mechanisms impacted by these drugs” and “[f]urther characterization is needed to determine risk factors associated with bothersome GI symptomatology.” *Id.*

Plaintiffs are correct that the *Lupianez-Merly Abstract* has not, to date, been published in full format or subjected to formal peer review. But “[p]ublication (which is but one element of peer review) is not the sine qua non of admissibility” and it “does not necessarily correlate with reliability.” *Daubert*, 509 U.S. at 593; *accord Oddi*, 234 F.3d at 145. Tellingly, Plaintiffs have not shown that this type of data is something that physicians would not ordinarily consider or that unpublished abstracts are necessarily unreliable. *See Adams v. United States*, Civ. No. 03–0049, 2009 WL 1085325, at \*3 (D. Idaho Apr. 19, 2009) (declining “to bar plaintiffs’ experts from offering any testimony that relies upon the conclusion in Dr. Morishita’s unpublished

sugar beet abstract that Oust causes damage to sugar beets at rates as low as 6 ppt”); *cf. Wade-Greaux v. Whitehall Labs., Inc.*, 874 F. Supp. 1441, 1470 (D.V.I. 1994) (“Dr. Tilelli relies upon anecdotal case reports, a type of data that is not relied upon by teratologists in making retrospective, cause-in-fact determinations.” (internal citation omitted)).<sup>35</sup> Nor have Plaintiffs identified any published studies that contradict Dr. Nguyen’s opinion or the results of the *Lupianez-Merly Abstract*. Indeed, the Court’s independent review of the submitted literature shows that—as the authors of the *Lupianez-Merly Abstract* note—in the GLP-1 RA context, additional research is needed to determine the prevalence of clinically significant delayed gastric emptying and its association with upper GI symptoms, if any. *See Jalleh 2024* at 960 (“Although GLP-1 RA-induced gastroparesis is generally accepted, how common it is remains unknown.”). And unlike Dr. Raines’s reliance on *Vijayvigara 2019*, *Coleski 2016*, and *Bi 2020*, Dr. Nguyen does not stretch the conclusions of the *Lupianez-Merly Abstract* further than the authors themselves are willing to go.

Instead, Plaintiffs focus on what they consider flaws in the parameters of the study discussed in the abstract. Specifically, Dr. Raines opines that the *Lupianez-Merly Abstract* is of little import here because the authors failed to exclude patients with preexisting GI symptoms and considered patients with only one GI symptom, including diarrhea and constipation, which

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<sup>35</sup> Plaintiffs argue that *Wade-Greaux* supports their argument that unpublished abstracts are unreliable bases for an expert’s opinion because the court in that case referred to an abstract as “anecdotal data.” (*See* Doc. No. 359 at 14.) But a review of the court’s opinion shows that it rejected the abstract as a reliable basis for the expert’s opinion because it discussed a chemical compound that was not found in either of the medications at issue. *Wade-Greaux*, 874 F. Supp. at 1470. Contrary to Plaintiffs’ suggestion, *Wade-Greaux* does not support the conclusion that all unpublished abstracts are necessarily “anecdotal evidence,” which automatically render an expert’s opinions unreliable.

are not typical of gastroparesis.<sup>36</sup> (Raines Rpt. at 12.) But these concerns go to the weight, not the admissibility, of Dr. Nguyen’s opinion, which relies on her extensive experience as a physician and researcher in the field of gastroenterology in addition to the *Lupianez-Merly Abstract*. See *Knight v. Avco Corp.*, No. 4:21-CV-00702, 2024 WL 3746269, at \*20 (M.D. Pa. Aug. 9, 2024) (finding “Avco’s suggestion that it is improper for Sommer to rely on publications which are not peer reviewed is unavailing,” and noting that in addition to these unpublished publications, “Sommer’s opinion is based upon his experience working with both Continental and Lycoming engines”).

Finally, it is relevant that Dr. Nguyen’s assertion that clinically significant delayed gastric emptying is rare among GLP-1 RA users is meant to support her overarching opinion on rebuttal that “gastrointestinal symptoms are not a reliable predictor of gastric emptying delay.” (Doc. No. 377 at 10; see also Doc. No. 359-1 at 13 (Plaintiffs acknowledging that Dr. Nguyen “leverages this opinion to conclude that ‘there has to be a different mechanism that is driving gastrointestinal symptoms’ in patients taking GLP-1RA drugs.” (cleaned up)); May 14, 2025 Pt. 2 Tr. at 144:16–24 (“So GLP-1s we know can delay gastric emptying. We also know that GLP-1s can cause symptoms of nausea and vomiting. What we don’t know in patients is whether or not the nausea and vomiting is due to delayed gastric emptying or other mechanisms or the delayed gastric emptying actually is causing the symptoms of nausea and vomiting. And the reason why you can’t make that leap between delayed emptying and symptoms and vice versa is that the symptoms are very nonspecific.”).) The *Lupianez-Merly Abstract* found that “[t]he distribution of GI symptoms among those with and without delayed [gastric emptying] was

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<sup>36</sup> Interestingly, and somewhat at odds with Dr. Raines’s assertions, the study found that there may be a correlation between delayed emptying and constipation. See *Lupianez-Merly, et al., Lupianez-Merly Abstract*, at S-1067.

similar except for constipation which was more common in those with delayed [gastric emptying].” *Lupianez-Merly Abstract* at S-1067. As Dr. Nguyen explained during the evidentiary hearing, these findings—that symptoms are not specific to delayed emptying—are “similar” to those she has seen in her own research (*see* May 14, 2025 Pt. 2 Tr. at 103:17–104:14 (discussing 2011 publication)), and those discussed in the published literature, *see* 2025 *Rome Consensus* at 70 (“[S]ymptoms of gastroparesis lack specificity . . . .”); *State of the Art* at 10 (“Side effects most reported with GLP-1 RAs are nausea, vomiting, and diarrhea . . . . Since these symptoms can occur in fasting subjects, they are probably not related to the effects of GLP-1 RA treatment on gastrointestinal functions (e.g., deceleration of gastric emptying) . . . .”); *Quast 2021* at 2351 (“The retardation of gastric emptying during GLP-1 RA treatment is unrelated to gastrointestinal symptoms.”); *cf. Jalleh 2024* at 961 (“The relationship between gastrointestinal symptoms and gastric emptying rate is weak . . . .”).

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Acknowledging that the *Lupianez-Merly Abstract* may have some limitations, the Court nevertheless declines to exclude Dr. Nguyen’s rebuttal opinion to the extent it relies on the results of the study discussed in the abstract. Importantly, although the full study is unpublished, Plaintiffs have not put forth any evidence to suggest physicians in the field would not consider such evidence in reaching their opinions. They also have not identified any medical or scientific literature that undermines or contradicts the abstract’s conclusions. To the contrary, the medical literature appears consistent with Dr. Nguyen’s overarching opinion that symptoms are a poor indication of whether a patient is suffering from delayed emptying. Finally, we note that Dr. Nguyen’s opinion was based not only on this abstract, but on her extensive experience as a practicing physician who regularly diagnoses gastroparesis and as a



leading expert in the field of gastroenterology. Accordingly, the Court declines to exclude Dr. Nguyen’s rebuttal opinion to the extent it rests on the *Lupianez-Merly Abstract* and/or the assertion that gastroparesis is rare among GLP-1 RA users.

### III. MOTION TO SUPPLEMENT

On July 23, 2025—more than two months after the Rule 702 hearing on the motions to exclude—Plaintiffs moved to supplement the record on Cross Cutting Issue No. 1 to include an October 2023 submission by Lilly to the FDA (the “FDA Submission”). (Doc. No. 447.) In the FDA Submission Lilly provides a cumulative review of the cases for severe/serious, prolonged, or worsening gastroparesis related to Trulicity. Plaintiffs argue that the should be considered by the Court in deciding the motions to exclude because in that context, Lilly told the FDA, “Gastroparesis is identified only in people who are presented for care, and it is documented by physician diagnosis, evaluating [gastric emptying] with scintigraphy, **or symptoms and retained food at endoscopy.**” (*Id.* at 1–2 (quoting Lilly Regulatory Response at LLY-GLPMDL-08233982 (Oct. 2, 2023) (emphasis added by Plaintiffs))). Plaintiffs assert that this statement, which was made in a formal submission to regulators, estops Lilly from taking a contrary position during this litigation. In other words, Plaintiffs ask the Court to consider the FDA Submission and find that it precludes Lilly from arguing that gastric emptying cannot be reliably diagnosed based on symptoms and the presence of retained gastric food. (*Id.* at 2.)

Lilly opposes the motion. (*See* Doc. No. 451.) It argues that the Court should deny the motion to supplement because Plaintiffs have been in possession of the FDA Submission for almost a year, yet they waited until the eleventh hour to provide it to the Court. (Doc. No. 451 at 6–8.) In the alternative, Lilly argues that even if the Court does consider the FDA Submission, estoppel should not occur because the statement identified by Plaintiffs is not

contrary to Lilly’s current litigation position. (*Id.* at 3–6.) For its part, Novo also opposes the motion to supplement, joining Lilly’s arguments and adding that the FDA Submission, even if considered, is irrelevant because it was not considered by any of the experts whose testimony is challenged by the motions to exclude. (Doc. No. 452.) Plaintiffs submitted a reply brief, reiterating their arguments. (Doc. No. 453.) And the Court heard oral argument on this issue during the July 29, 2025 monthly status conference.

Although the Court finds Defendants’ arguments in favor of denying the motion to supplement persuasive—especially Lilly’s argument that it will be prejudiced if the Court considers a document produced during fact discovery on a different issue in connection with Cross Cutting Issue No. 1, which was previously limited to expert discovery—we will nevertheless grant Plaintiffs’ request and consider the FDA Submission. Having reviewed the document in that context, the Court finds that estoppel is inappropriate, and regardless, nothing in the FDA Submission changes the Court’s finding that the conclusions of Drs. Raines and Siegel as to retained gastric food are unreliable.

To begin, as Lilly notes, it is far from clear that regulatory estoppel is an applicable doctrine in this circumstance. *See Chattanooga Prof. Baseball LLC v. Nat’l Casualty Co.*, No. 20-17422, 2022 WL 171936, at \*3 (9th Cir. Jan. 19, 2022) (“As for regulatory estoppel under federal law, the Teams cite no authority to adequately support the proposition that federal law recognizes regulatory estoppel. As for regulatory estoppel under state law, the Teams’ argument fails [because] the Teams acknowledge that of the ten states implicated in this appeal, only one has even arguably applied the doctrine of regulatory estoppel . . .”).

Nevertheless, even assuming this Court should apply the version of regulatory estoppel discussed by Plaintiffs and recognized by the Third Circuit when applying *Pennsylvania* law,

the Court does not find that doctrine warrants estoppel of Lilly’s arguments on the unreliability of retained gastric food as an indicator for delayed emptying. In Pennsylvania, “to support a claim for regulatory estoppel, a plaintiff must plead two elements: (1) A party made a statement to a regulatory agency; and (2) Afterward, the party took a position opposite to the one presented to the regulatory agency.” *Brian Handel D.M.D., P.C. v. Allstate Ins. Co.*, 499 F. Supp. 3d 95, 101 (E.D. Pa. 2020) (quotation marks omitted); *accord In re Suboxone (Buprenorphine Hydrochloride and Naloxone) Antitrust Litig.*, No. 13-MD-2445, 2017 WL 4810801, at \*8 (E.D. Pa. Oct. 25, 2017); *see also Hussey Copper, Ltd. v. Arrowood Indem. Co.*, 391 F. App’x 207, 211 (3d Cir. 2010) (“[U]nder Pennsylvania’s doctrine of regulatory estoppel, an industry that makes representations to a regulatory agency to win agency approval will not be heard to assert the opposite position when claims are made by litigants such as insured policyholders.” (cleaned up)).

For two reasons the Court does not find the FDA Submission contrary to Lilly’s litigation position in this case. First, it is important to understand the context of the sentence on which Plaintiffs rest their argument. It is one statement in the background section of a report that stretches more than 80 pages without exhibits and falls just shy of 550 pages with exhibits. Diagnosing gastroparesis was neither the focus of this report nor the objective of Lilly’s literature review. Moreover, the FDA Submission is just one of many reports submitted to the FDA at the same time as part of a packet of information. (*See* July 29, 2025 Hr’g Tr. at 15:23–18:23.)

Second, a holistic review of the FDA Submission shows it is consistent with Lilly’s position here that to measure gastric emptying, physicians must perform a gastric emptying study. Notably, under the section of the report titled “diagnosis,” Lilly states: “Gastroparesis

commonly is diagnosed by gastric scintigraphy, which measures emptying of a radiolabeled meal. A nonradioactive <sup>13</sup>C-labeled GE breath test is an alternative to scintigraphy.” (Doc. No. 447-2 at 15.) The statement referenced by Plaintiffs appears in a separate section titled “background epidemiology” and describes how some physicians find delayed emptying in cases when the patient suffers from type 2 diabetes and there is evidence of retained gastric food. (*Id.* at 18.) This statement is not inconsistent with Lilly’s position in this litigation because Lilly has acknowledged that some physicians will diagnose gastroparesis based on the presence of retained gastric food. (*See, e.g.*, July 29, 2025 Hr’g Tr. at 19:21–20:9.) Lilly disputes, however, that such a method is a *reliable* method for reaching such a diagnosis. Tellingly, in one of the other reports submitted to the FDA at the same time, Lilly represented to the FDA that the scientific literature suggests retained gastric food is *not* diagnostic of gastroparesis. (*See* July 29, 2025 Hr’g Tr. at 15:23–18:23 (discussing *Bi 2020* within a different report submitted at the same time).)

In sum, when Lilly’s statement—“[Gastroparesis] is documented by physician diagnosis, evaluating [gastric emptying] with scintigraphy, or symptoms and retained food at endoscopy.”— is considered in context, the Court cannot say that the company took an affirmative position on how to reliably diagnose gastric emptying or gastroparesis, let alone one that is contrary to its current litigation position.

#### IV. CONCLUSION

For the reasons stated above, the Court grants Plaintiffs’ motion to supplement and Defendants’ motions to exclude the opinions of Drs. Raines and Siegel made in connection with Cross Cutting Issue No. 1. The Court denies Plaintiffs’ partial motion to strike the opinions of Dr. Nguyen. As a result of this ruling, any plaintiff claiming to have had drug-induced

gastroparesis must have had a gastric emptying study (scintigraphy, breath test, or WMC) properly performed at the time of diagnosis, which confirmed delayed emptying. In truth, this holding will have relatively little effect on the vast majority of the cases in this MDL because most Plaintiffs claim to have permanent/persistent gastroparesis, not temporary, drug-induced gastroparesis. As previously noted, Plaintiffs' counsel have repeatedly conceded that a properly performed gastric emptying study (scintigraphy, breath test, or WMC) is necessary for a physician to reliably diagnose all subsets of gastroparesis other than temporary, drug-induced gastroparesis. (*See* May 16, 2025 Hr'g Tr. at 15:3–12 (Plaintiffs' counsel agreeing that “permanent gastroparesis as a diagnosis” requires a gastric emptying study); July 29, 2025 Hr'g Tr. at 13:15–23 (“Mr. Buxner: . . . Like both experts agreed, Dr. Raines and Dr. Nguyen, if a patient is pulled from the GLP-1 RA . . . and the symptoms persist, then a GES would be ordered to see what is going on. The Court: Okay. And you agree with that? Mr. Buxner: Oh I agree with that.”).)

Nevertheless, the Court recognizes that given this ruling, some Plaintiffs in this MDL will be unable to prove that they suffered from gastroparesis because their diagnosis was not based on a properly performed gastric emptying study. Although unfortunate, it would be perhaps more unjust to hold Defendants potentially liable for damages based on an unreliable diagnosis. For that reason, courts in other cases have rejected similar claims where the plaintiffs were unable to prove the cause of their illness because their treating physician failed to perform a necessary test at the time of diagnosis. *See In re: Zostavax*, 711 F. Supp. 3d 317, 320–21 (E.D. Pa. 2022) (finding a subset of plaintiffs' claims would fail for want of proof because their physicians failed to perform a PCR test and “the record is undisputed that such testing is the only way to prove whether Zostavax or the wild-type virus caused a person's shingles.

Otherwise, causation in any case is mere speculation”); *Buzzerd v. Flagship Carwash of Port St. Lucie, Inc.*, 669 F. Supp. 2d 514, 531 (M.D. Pa. 2009) (“Undoubtedly, the healthcare professionals in this case are hampered in their ability to perform a proper differential diagnosis by the absence of objective testing to confirm their causation hypothesis, such as carboxyhemoglobin results. But the uncertainty caused by the absence of objective testing is not to be borne by Defendants.”); *cf. In re Nat’l Football League Players Concussion Injury Litig.*, No. 23-1585, 2025 WL 560631, at \*1–2 (3d Cir. Feb. 20, 2025) (finding the district court reasonably read scientific sources to conclude “a Death with CTE diagnosis can be made only after examining brain tissue under a microscope”).

An appropriate order follows.